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Exposure to combustion of solid fuel and tuberculosis: a matched case–control study

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ABSTRACT: The present study was conducted in Benin to ascertain the association between exposure to combustion of solid fuel (coal and biomass) and tuberculosis.

Cases were consecutive, sputum smear-positive tuberculosis patients never previously treated for tuberculosis for as long as 1 month. Two controls were selected from the neighbourhood of each case, matched by age and sex by a predefined procedure.

A total of 200 new smear-positive cases and 400 neighbourhood controls were enrolled. In univariate analysis, using solid fuel for cooking (OR 1.7, 95% CI 1.1–2.8), ever smoking (OR 5.5, 95% CI 3.1–9.8), male sex (OR 10.5, 95% CI 1.6–71.1), daily use of alcoholic beverages (OR 2.3, 95% CI 1.2–4.2) and having a family member with tuberculosis in the previous 5 yrs (OR 30.5, 95% CI 10.8–85.8) were all significantly associated with tuberculosis cases. When all significant variables were entered into a multivariate conditional logistic regression model, the association between using solid fuel for cooking and tuberculosis cases was no longer statistically significant (adjusted OR 1.4, 95% CI 0.7–2.7).

In conclusion, the association between exposure to combustion of solid fuel and tuberculosis was relatively weak and not statistically significant.

KEYWORDS: **Biomass, fossil fuels, indoor air pollution, risk factors, tuberculosis**

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BARIS and EZZATI [1] have presented the case for linking interventions to control tuberculosis, tobacco and biomass fuel smoke exposure as a means of improving the efficiency of health services [2]. While substantial evidence links tobacco smoke exposure with tuberculosis [3–6], evidence for the link with exposure to the smoke of solid fuel (coal and biomass) is more scarce [7–9]. SLAMA *et al.* [7] recently conducted a systematic review of indoor solid fuel combustion and tuberculosis. They reported that three (50%) of the six studies [8–10] showed a significant effect and concluded that despite the plausibility of an association, available original studies did not provide sufficient evidence of an excess risk of tuberculosis due to exposure to indoor solid fuel combustion.

The comprehensive lung health project, funded by the World Bank and implemented by the International Union Against Tuberculosis and Lung Disease, aimed to reduce the burden of lung disease in selected communities through improvement in the case management of priority cases and through interventions to reduce exposures to harmful agents. As part of the project, the prevalence of exposure to smoke from solid fuels used in dwellings was determined for tuberculosis patients. To investigate whether exposure to combustion of solid fuel is significantly associated with tuberculosis, a protocol proposed to estimate risk for tuberculosis associated with this exposure was developed and conducted in Benin. We report the results of the study.

METHODS

The present study was a matched case–control study to investigate the association between exposure to combustion of solid fuel and tuberculosis.

Site of the study

The study was conducted in Benin in 2008. The estimated incidence of smear-positive tuberculosis cases in Benin was 39 per 100 000 population [11] and the number of new smear positive cases reported in 2007 was 2,770. This study was conducted in the largest tuberculosis management unit in the city of Cotonou.

Study population

Cases were consecutive, sputum smear-positive tuberculosis patients aged $\geqslant$15 yrs presenting to health facilities in Cotonou who had never been previously treated for tuberculosis for as long as 1 month. As sputum culture for *Mycobacterium tuberculosis* was not routinely performed in Benin and the quality in the diagnosis

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of smear-negative tuberculosis may not be consistent, only smear-positive tuberculosis cases were included.

Two controls were selected from the neighbourhood of each case, matched by age and sex by predefined procedures. Briefly, two households were randomly selected in the community where the cases lived, with interview of one subject from each of the two houses. The last digit (*n*) of the case's registration number was used for selection of the control household. If *n* was an even number, the *n*th and $(n+1)$th neighbouring house to the right of patient's house was selected as the first and the second control. If the *n*th or the $(n+1)$th neighbouring house refused to participate in the study, the next $(n+2$, $n+3$, *etc.*) neighbouring house to the right was selected. until two neighbouring houses were recruited. If *n* was an odd number, the neighbouring house to the left of the patient's house was selected following the same principle.

Selection of the control from each neighbouring house

One informant was selected from each neighbouring house. Any family member of the same sex and similar age (within the range of ±15 yrs of age) as the patient was of priority to be selected as a control. If there was more than one priority control in the house, one was selected randomly. If there was no such family member in the neighbouring house or if the person of the same sex and similar age was unavailable or refused to participate in the study, any family member was randomly selected for interview.

Sample size

The required sample size was estimated using the following assumptions: 1) prevalence of exposure in those without disease (controls) ⩾20%; and 2) odds ratio of importance ⩾2.0. Applying a 95% two-sided confidence interval and 80% power, the number of participants required to satisfactorily address the hypothesis, given the assumptions, was 137 cases and 274 controls [12]. Recruitment of participants started in June 2008 and continued until 200 tuberculosis patients and 400 controls had agreed to participate, to account for the effects of other variables (such as tobacco smoking) as well as missing information, for whatever reason.

Patients were considered ineligible if they did not sign the consent form to be interviewed or did not allow the researchers to contact their neighbour.

After informed consent had been obtained, the research technician administered a questionnaire containing questions on demographic information, smoking habits and use of solid fuel for cooking or heating. The questions concerning solid fuel use were selected from an internationally recommended questionnaire for use in national prevalence surveys for tuberculosis [13]. Solid fuel included coal/lignite, charcoal, wood, straw/shrubs/grass, animal dung and agricultural crop residue; nonsolid fuel included electricity, liquefied petroleum gas, natural gas, biogas and kerosene. A household that used solid fuel either for cooking and/or heating was classified as being exposed to combustion of solid fuel (indoor air pollution). Other questions included any family member living in the house diagnosed with tuberculosis in past 5 yrs, frequency and amount of consumption of drinking alcoholic beverages, smoking behaviour, exposure to the tobacco smoke of others, type of stove used for cooking, use of a hood or chimney, location of cooking, and ventilation in cooking area.

Data were double entered and validated using EpiData Entry 3.1 (EpiData Association, Copenhagen, Denmark). STATA version 8.0 (StataCorp, College Station, TX, USA) was used for statistical analysis. Odds ratios and their corresponding 95% confidence intervals for categorical variables were determined by Mantel–Haenszel estimate to combine the information from each matched group [14]. Three approaches were undertaken to address missing values. First, analysis was performed for individuals without missing values. Secondly, individuals with missing values were assumed to be unexposed and comparison of exposed *versus* unexposed/unknown was performed. Thirdly, individuals with missing values were assumed to be exposed and comparison of exposed/unknown *versus* unexposed was performed. In addition, a fourth approach was undertaken to address missing values in multivariate analysis, including an unknown category of each variable. A p-value <0.05 was considered statistically significant. All significant variables were entered into a multivariate conditional logistic regression model and a final fitted model was determined by backward elimination methods. Finally, propensity scores were included in the model to control for potential selection bias by using STATA version 11 [15].

The study was reviewed and approved by the Union Ethics Advisory Group (Paris, France).

RESULTS

A total of 200 new smear-positive cases and 400 neighbourhood controls were enrolled. Table 1 shows age, sex and other characteristics of cases and controls. The mean age among tuberculosis cases was 35.2 yrs. The male/female ratio among tuberculosis cases was 2.4. The proportion of tuberculosis cases with any family member having been diagnosed with tuberculosis in the previous 5 yrs was 32%, which was much higher than that of controls (3.5% for first controls and 1.5% for second controls). The proportion of ever-smokers among tuberculosis cases (26%) was much higher than that of controls (7% for first controls and 6% for second controls). Of the 78 ever-smokers, 76 provided information on the age when they started smoking. Of these 76 ever-smokers, 12 (15.8%) started smoking at age <15 yrs, 24 (31.6%) at age 15–19 yrs, 18 (23.7%) at age 20–24 yrs and 22 (29.0%) at age ⩾25 yrs. Of the 52 ever-smokers among tuberculosis cases, five (9.6%) were current smokers, 44 (84.6%) did not smoke in past month and three (5.8%) did not provide an answer. Of the 14 ever-smokers among first controls, six (42.9%) were current smokers, six (42.9%) did not smoke in past month and two (14.3%) were unknown. Of the 12 ever-smokers among second controls, four (33.3%) were current smokers, six (50.0%) did not smoke in past month and two (16.7%) were unknown. The proportion of tuberculosis cases who used alcoholic beverages daily was 12.5%, and that among controls was less (7% for first controls and 6% for second controls).

Table 2 shows the type of fuels used. The majority used charcoal/coal/lignite (74% of cases, 74% of first controls and 68.5% of second controls) and a small minority used biomass, *i.e.* wood/straw/shrubs/grass, animal dung or agricultural crop residue (15% of cases, 11.5% of first controls and 10.0% of

TABLE 1 Characteristics of cases and controls

	Case	First control	Second control
Total	200 (100)	200 (100)	200 (100)
Age# yrs	35.2±13.2	34.6±12.7	34.7±11.9
Sex¶			
Male	139 (69.5)	130 (65.0)	126 (63.0)
Female	59 (29.5)	68 (34.0)	69 (34.5)
Unknown	2 (1)	2 (1)	5 (2.5)
Family member with tuberculosis in past 5 yrs* **			
Yes	64 (32.0)	7 (3.5)	3 (1.5)
No	135 (67.5)	193 (96.5)	196 (98.0)
Unknown	1 (0.5)	0	1 (0.5)
Solid fuel for cooking+			
Yes	178 (89.0)	171 (85.5)	157 (78.5)
No	21 (10.5)	28 (14.0)	42 (21.0)
Unknown	1 (0.5)	1 (0.5)	1 (0.5)
Ever smoked***			
Yes	52 (26.0)	14 (7.0)	12 (6.0)
No	146 (73.0)	186 (93.0)	183 (91.5)
Unknown	2 (1.0)	0.0	5 (2.5)
Daily use of alcohol beverage§			
Yes	25 (12.5)	14 (7.0)	12 (6.0)
No	167 (83.5)	183 (91.5)	178 (89.0)
Unknown	8 (4.0)	3 (1.5)	10 (5.0)

Data are presented as n (%) or mean±SD. #: p=0.883; ¶: p=0.463; +: p=0.064; §: p=0.037; ***: p<0.001.

second controls). Together, the proportion of study participants who used solid fuel for cooking was 89% of tuberculosis cases, 85.5% of first controls and 78.5% of second controls. Only two participants who used solid fuel for heating also used solid fuel for cooking. Table 3 shows the types of stove used, location and ventilation among those who used solid fuel for cooking. Only a very small minority used open or surrounded fires for cooking; the majority used improved single-pot stoves. Only a very small number of participants cooked in a room used for living/sleeping; the majority cooked in a separate room/building or outdoors. When cooking indoors, only five participants cooked in a closed room and a minority used a room with roof spaces; the majority used a room with windows/doors.

TABLE 2 Type of fuels used by study participants#

	Case	First control	Second control
Total	200 (100.0)	200 (100.0)	200 (100.0)
No food cooked at home	4 (2.0)	1 (0.5)	0
Electricity	0	1 (0.5)	0
Liquefied petroleum gas	2 (1.0)	0	1(0.5)
Natural gas	12 (6.0)	22 (11.0)	35 (17.5)
Kerosene	3 (1.5)	4 (2.0)	6 (3.0)
Coal/lignite	0	0	1 (0.5)
Charcoal	148 (74.0)	148 (74.0)	136 (68.0)
Wood/straw/shrubs/grass	29 (14.5)	21 (10.5)	18 (9.0)
Animal dung	0	0	1 (0.5)
Agricultural crop residue	1 (0.5)	2 (1.0)	1 (0.5)
Unknown	1 (0.5)	1 (0.5)	1 (0.5)

Data are presented as n (%). #: p=0.072.

Table 4 shows results of univariate analysis. Among individuals without missing values, using solid fuel for cooking (OR 1.7, 95% CI 1.1–2.8), ever smoking (OR 5.5, 95% CI 3.1–9.8), male sex (OR 10.5, 95% CI 1.6–71.1), daily use of alcohol beverages (OR 2.3, 95% CI 1.2–4.2) and having a family member with tuberculosis in the previous 5 yrs (OR 30.5, 95% CI 10.8–85.8) were all significantly associated with tuberculosis cases. As the number of individuals with missing values was small, analysis comparing exposed *versus* unexposed/unknown and comparing exposed/unknown *versus* unexposed among all participants provided consistent odds ratios of all variables listed in table 4 with significant association with tuberculosis. In terms of cooking practice, cooking by open/surrounded fire was not significantly associated with tuberculosis (OR 1.8, 95% CI 1.0–3.1); cooking in a closed room/room with roof spaces was also not significantly associated with tuberculosis (OR 1.3, 95% CI 0.8–2.1).

The analysis of using solid fuel for cooking was further stratified by sex; the association between using solid fuel for cooking and tuberculosis remained significant among males (OR 1.8, 95% CI 1.0–3.2; p=0.042) but was not significant among females (OR 2.5, 95% CI 0.9–7.0). Table 5 shows the results of multivariate analysis. When all significant variables

TABLE 3 Type of stove used, and location and ventilation among those who used solid fuel for cooking

	Case	First control	Second control
Total	178 (100)	171 (100)	157 (100)
Type of stove used for cooking#			
Open fire	11 (6.2)	6 (3.5)	8 (5.1)
Surrounded fire	11 (6.2)	11 (6.4)	4 (2.6)
Improved single-pot stove	151 (84.8)	153 (89.5)	144 (91.7)
Improved multiple-pot stove	3 (1.7)	0	0
Unknown	2 (1.1)	1 (0.6)	1 (0.64)
Smoke removed by hood or chimney¶			
Yes	1 (0.6)	0	0
No	174 (97.8)	170 (99.4)	155 (98.7)
Unknown	3 (1.7)	1 (0.6)	2 (1.3)
Location of cooking+			
In a room used for living/sleeping	5 (2.8)	2 (1.2)	1 (0.6)
In a separate room	42 (23.6)	56 (32.8)	47 (29.9)
In a separate building	10 (5.6)	15 (8.8)	15 (9.6)
Outdoors	81 (45.5)	73 (42.7)	70 (44.6)
Other	40 (22.5)	25 (14.6)	24 (15.3)
Ventilation at location of cooking§			
Closed room	3 (1.7)	1 (0.6)	1 (0.6)
Room with roof spaces	27 (15.2)	22 (12.9)	25 (15.9)
Room with open windows/doors	20 (11.2)	31 (18.1)	24 (15.3)
Room with ≤3 walls	4 (2.3)	4 (2.3)	0
Outdoors	81 (45.5)	73 (42.7)	70 (44.6)
Other	29 (16.3)	25 (14.6)	25 (15.9)
Unknown	14 (7.9)	15 (8.8)	12 (7.6)

Data are presented as n (%). #: p=0.223; ¶: p=0.596; +: p=0.189; §: p=0.716.

TABLE 4 Mantel–Haenszel estimate of the odds ratio controlling for matched groups

	Participants n	OR (95% CI)	Chi-squared	p-value
Solid fuel for cooking				
Yes *versus* no	597	1.7 (1.1–2.8)	5.23	0.0222
Yes *versus* no/unknown	600	1.7 (1.1–2.7)	5.03	0.0250
Yes/unknown *versus* no	600	1.7 (1.1–2.8)	5.23	0.0222
Ever smoked				
Yes *versus* no	593	5.5 (3.1–9.8)	43.44	<0.0001
Yes *versus* no/unknown	600	5.6 (3.2–9.9)	44.74	<0.0001
Yes/unknown *versus* no	600	4.9 (2.8–8.3)	40.61	<0.0001
Sex				
Male *versus* female	591	10.5 (1.6–71.1)	9.02	0.0027
Male *versus* female/unknown	600	6.5 (1.7–25.3)	9.68	0.0019
Male/unknown *versus* no	600	5.8 (1.4–23.0)	7.85	0.0051
Daily use of alcoholic beverages				
Yes *versus* no	579	2.3 (1.2–4.2)	6.80	0.0091
Yes *versus* no/unknown	600	2.2 (1.2–4.1)	6.40	0.0114
Yes/unknown *versus* no	600	1.9 (1.1–3.1)	5.98	0.0145
Family member with tuberculosis in past 5 yrs				
Yes *versus* no	598	30.5 (10.8–85.8)	102.38	<0.0001
Yes *versus* no/unknown	600	30.5 (10.8–85.8)	102.38	<0.0001
Yes/unknown *versus* no	600	24.8 (9.8–62.9)	101.15	<0.0001

TABLE 5 Multivariate conditional logistic regression controlling for age

	OR (95% CI)	SD	z-score	p-value
Solid fuel for cooking	1.4 (0.7–2.7)	0.47	0.89	0.37
Ever smoking	4.2 (2.0–8.7)	1.56	3.84	<0.01
Male sex	3.3 (0.7–16.0)	2.67	1.51	0.13
Daily use of alcoholic beverages	1.7 (0.8–3.9)	0.71	1.30	0.19
Family member with tuberculosis in past 5 yrs	36.4 (11.1–119.3)	22.05	5.93	<0.01

were entered into a multivariate conditional logistic regression model, ever smoking and having a family member with tuberculosis in the previous 5 yrs were significantly associated with tuberculosis cases; the association between using solid fuel for cooking and tuberculosis cases was relatively weak and no longer statistically significant (adjusted OR 1.4, 95% CI 0.7–2.7; p=0.372). Including propensity score in the model showed a similar result (adjusted OR 1.4, 95% CI 0.7–2.7; p=0.357). The most parsimonious model included ever smoking (OR 6.5, 95% CI 3.3–12.9) and having a family member with tuberculosis in the previous 5 yrs (OR 33.4, 95% CI 11.6–95.9), which were significantly associated with tuberculosis. The association between using solid fuel for cooking and tuberculosis was also not statistically significant in models comparing exposed *versus* unexposed/unknown (OR 1.4, 95% CI 0.7–2.6), comparing exposed/unknown *versus* unexposed (OR 1.3, 95% CI 0.7–2.6) and including unknown as a category of each variable (OR 1.4, 95% CI 0.7–2.7) among the whole cohort (data not shown). When the analysis was restricted to males, the association between using solid fuel for cooking and tuberculosis was also not statistically significant after controlling for other variables (data not shown).

Even if the cooking fuels were grouped into biomass fuels and other fuels, as in the study by MISHRA *et al.* [8], using biomass fuel for cooking (OR 1.5, 95% CI 0.9–2.3; p=0.13) was not significantly associated with tuberculosis.

DISCUSSION

The burning of solid fuels for cooking and heating is probably the largest source of indoor air pollution [16]. It has been estimated that 50% of the global population (~3 billion people) use biomass fuels for domestic cooking, lighting and heating [17]. Solid fuels are classified as low-efficiency fuels and release many pollutant products when they are burnt. The evidence that acute respiratory infections in children and chronic obstructive pulmonary disease (COPD) in females are associated with exposure to indoor solid fuel smoke has been judged to be strong. There is also a clear association between lung cancer in females and household coal use. However, evidence for the association with tuberculosis in adults is considered scarce.

The association between exposure to combustion of solid fuel and tuberculosis has been previously reported. GUPTA *et al.* [10] performed a study to investigate environmental risk factors of respiratory disease. Those who used wood and cow dung cakes were significantly more likely to have tuberculosis compared with those who used kerosene or gas (OR 2.5, 95% CI 1.1–16.0), but the authors only controlled for age in their analysis. MISHRA *et al.* [8] used data from India's 1992–1993 National Family Health Survey to investigate biomass cooking fuels and prevalence of tuberculosis in India. Cooking fuels were categorised into two groups: biomass fuels (wood or dung) and cleaner fuels (charcoal, coal/coke/lignite, kerosene, electricity, petroleum gas or biogas). They reported that cooking using biomass fuels is significantly associated with tuberculosis (adjusted OR 2.6, 95% CI 2.0–3.4), compared with cooking using cleaner fuel. However, they did not control for smoking in the analysis. PÉREZ-PADILLA *et al.* [9] conducted a case–control study in Mexico City (Mexico). Current exposure to biomass smoke was significantly associated with active tuberculosis for the Mexico City metropolitan area and central Mexico after adjusting for smoking and other variables (adjusted OR 2.4, 95% CI 1.0–5.6). However, another three studies identified by SLAMA *et al.* [7] did not report consistent association between usage of solid fuel and tuberculosis [18–20]. Recently, a nested case–control study in India reported adjusted OR 1.7 (95% CI 1.0–2.9) for biomass usage and tuberculosis [21].

It is common that females spend more time cooking and are more likely to be affected by combustion of solid fuel than males. However, there is no consistent evidence demonstrating that tuberculosis in females is associated with exposure to combustion of solid fuel. MISHRA *et al.* [8] reported adjusted OR 2.7 (95% CI 1.9–4.1) and PÉREZ-PADILLA *et al.* [9] reported adjusted OR 6.6 (95% CI 2.9–14.0) among females for the association between biomass cooking fuels and tuberculosis. However, CRAMPIN *et al.* [18] reported that there was no association between cooking fire exposure and tuberculosis in females. In the present study in Benin, the association between use of biomass fuel for cooking was not significantly associated with tuberculosis in females when the analysis was stratified by sex. Furthermore, although using solid fuel for cooking was significantly associated with tuberculosis cases in univariate analysis, the association was not statistically significant after controlling for other variables in multivariate analysis. Determinants significantly associated with tuberculosis were ever smoking and having a family history of tuberculosis, which was not a surprising finding. There have been numerous published studies reporting that smoking is associated with tuberculosis [4–6, 22–27] and that family contacts are at high risk of tuberculosis [28–32]. The question is why usage of solid fuel for cooking was not significantly associated with tuberculosis in the study population, even among females.

As MISHRA *et al.* [8] pointed out, fuel type may not be an ideal measure of exposure to smoke. The amount of indoor air pollution that is created when biomass is burned depends on several factors, mainly related to the characteristics of combustion. The amount of smoke released during burning and the efficiency of removing the smoke through ventilation determine the concentration of smoke. The total exposure to the smoke, in turn, is determined by both the concentration of smoke and the duration of exposure [33]. Indoor air pollution could be minimised if an adequate stove with proper ventilation was used, and could be very bad if high-pollution solid fuels were burning on open stoves with poor ventilation [34].

Among participants of the present Benin study, the concentration of smoke generated when solid fuel was used for cooking was probably low, because the majority of participants used an improved single-pot stove and cooked in a separate room/building with windows/doors or outdoor. This probably explains why the association between usage of solid fuel and tuberculosis was not significant in this study population. If this is the case, this negative finding probably indicates that reducing indoor air pollution may be helpful in tuberculosis control [2]. Even though the association between use of solid fuel and tuberculosis is not consistent, there has been sufficient evidence of a harmful effect of combustion of solid fuels to take action. People need to be educated about the harmful effects of combustion of solid fuels (acute respiratory infection, lung cancer, COPD, *etc.*) and be advised to modify cooking practice to keep indoor air pollution low, such as keeping a distance when there is most pollution (in early stages of burning), burning outdoors, using a separate space for cooking and improving ventilation by keeping windows and doors open [33]. If funding is available, implementing an improved cooking stove programme [8] may be considered before transition to clean fuels is possible.

The strength of our study was that there was a clear tuberculosis case definition and exposure to combustion of solid fuel was assessed by a structured, standardised questionnaire. One of the limitations of this study was that there were a few participants with missing values. However, the number of participants with missing values was small. We applied four approaches to deal with missing values and the findings of these approaches were consistent. Although we did not apply imputation techniques to estimate the values of missing covariates, analysis using imputation data is not likely to change the finding of our analysis.

In conclusion, the present study conducted in Benin did not confirm the association between domestic usage of solid fuel and tuberculosis. Further study on this subject is needed. However, intervention to reduce indoor air pollution should not be delayed by this negative finding.

SUPPORT STATEMENT

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STATEMENT OF INTEREST

None declared.

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