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MAIN RESEARCH ARTICLE

Higher risk of stillbirth among lower and middle income women who do not use tobacco, but live with smokers

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Abstract

Objective. To investigate pregnancy outcomes among women living with smokers. *Design.* Data were from a cohort study of 1,217 women recruited during 3–7th month of pregnancy and 96% followed-up after delivery. The main objective was to investigate effects of smokeless tobacco on pregnancy outcomes. *Setting.* Lower and middle-class neighborhoods in Mumbai, India. Community health volunteers who had good rapport with the local population collaborated with the study personnel to help locate and interact with potential participants. *Population.* Singleton births from non-tobacco users; $n = 924/903/802$ for stillbirth/gestational age/birthweight analysis. Non-smoking women who lived with smokers (28%) were categorized as 'exposed' to second hand smoke (SHS). *Methods.* House-to-house surveys with questionnaire administration and medical records abstraction by trained personnel at recruitment and follow-up. *Outcome measures.* Stillbirth (no evidence of life at birth after at least 20 weeks of gestation), low birthweight (≤ 2,499 g) and preterm birth (≤ 258 days of gestation). *Results.* Rates of low birthweight and preterm birth were not significantly different between exposed and non-exposed. Hazard ratio for stillbirth in SHS exposed women ($n = 261$) was 2.2 (95% confidence interval 1.1–4.4). Survival times differed significantly between exposed and non-exposed, $p = 0.012$. Exposed and non-exposed groups differed significantly by education, socioeconomic status, parity and access of antenatal care. After adjustment for these potential confounders in Cox proportional hazards models (gestational age in days as timescale), hazard ratios for stillbirth in the exposed group remained unchanged: 2.1 (1.1–4.3). *Conclusions.* Pregnant women living with smokers in their household have a significantly higher risk of stillbirth, independent of differences in socio-demographic characteristics and antenatal care.

Key words: *Second hand smoke, passive smoking, stillbirth, pregnancy, cohort*

Introduction

The poor impact of maternal direct or active smoking on reproductive perinatal outcomes is well documented, including spontaneous abortions, reduction in mean birthweight, increased risk of 'small for gestational age', preterm birth, perinatal death and Sudden Infant Death Syndrome (1).

The impact of second hand smoke (SHS) on perinatal outcomes is, however, less clear with relatively sparse data compared with the evidence for direct smoking. Furthermore, these data yield contradictory results. In 1967, Comstock and Lundin (2) reported no significant differences in stillbirth rates by paternal smoking status. Their result was consistent with Ahlborg and Bodin who reported an odds ratio of 1.06 (95% confidence interval (CI) 0.55–2.05) for intrauterine fetal loss in non-smoking women exposed to SHS at home (3). In contrast, Mau and Netter 1974 (4) reported slightly higher stillbirth rates with heavier paternal smoking (relative risk = 1.2 with more than 10 cigarettes/day). While two recent reviews (5,6) and the California Environmental Protection Agency report sufficient evidence for a causal

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association of SHS with preterm delivery (7), the 2006 US Surgeon General's report states that evidence is suggestive but not sufficient to infer a causal relation (8).

Meta-analyses pooled estimates indicate a small reduction in mean birthweight ranging from 25 to 40 g and relative risks ranging from 1.2 to 1.4 for both low birthweight (defined as births of babies weighing less than 2,500 g) and intra-uterine growth restriction (7–9).

Much of the evidence on the relation between SHS and reproductive outcomes is from developed countries with little information from middle and lower income countries. Although the prevalence of smoking among women is often lower relative to men, there is substantial evidence that women from low and middle income countries who do not smoke live in environments where they are subjected to high rates of SHS (10). Understanding the impact of SHS on reproductive health outcomes is therefore important to develop appropriate interventions and to argue for appropriate resources to improve the health not only of the mothers and their children but also of all family members and co-workers who expose the women and children to a higher risk of poor health.

This paper reports on birthweight, gestational age at birth and stillbirth in women who do not use any form of tobacco but who live with smokers from a cohort study in Mumbai, India. Although this study was carried out with the primary objective of investigating the effect of smokeless tobacco use on reproductive outcomes (11,12), the data collected also allowed an investigation of outcomes in non-tobacco using women living with cigarette or bidi (South Asian leaf wrapped cigarette type) smokers.

Material and methods

Primary care to pregnant women in Mumbai is provided through 180 Corporation Health Posts. We selected eight health posts, four in the main city area and four in the outskirts of the city for our study. These health posts were a convenience sample based on interest of health post staff to collaborate. Community health volunteers (CHVs) attached to these health posts provided willing and enthusiastic support to the study, helping the study personnel to locate and interact with potential study participants. CHVs usually belong to the same communities which they serve, tend to have a good rapport with women in their respective areas and make regular house-to-house visits to provide health education and to increase contact of the population with the health care system, particularly during pregnancy and after birth. Their work is usually limited to lower and middle class women.

CHVs were requested to list all pregnant women in their respective areas before start of field study. The survey field staff visited the homes of the pregnant women accompanied by the CHVs and screened potential participants for eligibility (defined as women between 3 and 7 months pregnant and who intended to live in the study area after delivery). All women who were contacted consented to participate. Oral consent was sought and obtained from each participant after they were explained the purpose of the study. Most recruited women were followed-up within a month of the birth.

At recruitment, a pilot-tested questionnaire was used to seek information on socio-demographic factors, obstetric history, exposure to smoking, tobacco and alcohol use. The information collected included maternal age, education and paid employment history of the respondent, the occupation of the woman's husband, household income, parity, previous history of stillbirth and self-reports of any medical conditions. A composite measure of socio-economic status was derived from incorporating the occupational status of the father of the unborn child and the per-capita income of the family (12). Weight of the women at recruitment was measured using a bathroom weighing scale (pre-pregnancy weight was generally not known). Height was marked out with the women standing against a straight wall and measured accurately with an inch tape. Medical records of the birth, ultrasound and lab reports were abstracted.

Exposure to tobacco smoke was assessed at recruitment using the following questions.

- 'How many persons in your household smoke bidi or cigarettes?'
- 'If you take up paid work, generally how many persons are smoking bidi or cigarettes in your vicinity?'

Exposure to tobacco smoke was assessed at follow-up using the following question.

- 'Does anyone smoke bidi or cigarettes inside your home?'

These smoking persons could include the husband of the pregnant woman, brother/s, father, father-in-law or other relatives resident in the same household (women in the study area generally did not smoke); information was not sought on the number of cigarettes/bidis smoked.

Non-tobacco using women who reported smoking by household members or who reported being exposed to SHS at their workplace formed the 'exposed' group. Non-tobacco using women who

reported no smoking by household members or who were not exposed at work were defined as 'non-exposed'. Positive responses either at recruitment or follow-up were taken to indicate exposure (3% of women who had not reported smoking by family members at recruitment reported indoor smoking practices at follow-up).

Medical, sonography and laboratory records were abstracted to supplement information obtained from the interview, including number of antenatal visits for the index pregnancy, number of tetanus toxoid (TT) doses received by the pregnant woman, HIV status, hemoglobin levels, any obstetric/medical conditions and gestational age. Receiving two or three doses of TT was considered as an indicator of better quality of antenatal care. None of the women used alcohol; none of the women with available HIV test reports ($n = 420$) had positive results. Categorizations were as in Table 1; age of mother and parity had three categories (two of which are in Table 1), and all other variables had two categories (the category thought to be at greater risk is given in Table 1). Chi-squared tests were used to estimate the significance of differences in these factors between exposed and non-exposed groups.

Birthweight and gestational age of the infant and date of delivery were abstracted from the infant immunization card or delivery records. Birth records from two large government hospitals in the study area were also abstracted. Low birthweight was defined as ≤ 2,499 g. Gestational age was calculated in number of days from the date of start of the last normal menstrual period to the date of delivery; this was reasonably consistent with ultrasound estimates where available (10). Preterm birth was defined as birth of ≤ 258 days (37 weeks) of gestation. Anemia was defined as a hemoglobin level < 10 g%.

Stillbirth was defined as a newborn who did not breathe or show any other evidence of life at birth after at least 20 weeks of gestation. Sympathetic and careful questioning on whether the newborn breathed moved or cried after birth and for how many hours/days the baby was alive was used to distinguish between live-births, stillbirths and neonatal deaths. Hospital ascertainment of stillbirths was not possible as the women delivered in at least 30 different government and private hospitals in and around the study area. We avoided asking the mother for death certificates to avoid upsetting the mother; also stillbirths are sometimes not registered by their families. Complete data on perinatal/neonatal deaths were lacking (many women were followed-up within a week/month of birth).

In the recruitment phase, 1,217 pregnant women provided oral informed consent for participation. Of these, 50 could not be later contacted further yielding a total of 1,167 (96%) of the recruited pool who could be administered the structured questionnaire. An additional 236 women were excluded: abortions (before 20 weeks) ($n = 11$), neonatal deaths ($n = 11$), bidi smokers ($n = 2$), smokeless tobacco users ($n = 208$); women with diabetes, mitral stenosis or

Table 1. Characteristics (n, %) of exposed (denominator = 261 unless otherwise specified) and non-exposed women (denominator = 663 unless otherwise specified).

Characteristics and outcomes	Non-exposed	SHS exposed
Age		
≤ 20 Years	119 (17.9)	47 (18)
≥ 30 Years	83 (12.5)	29 (11.1)
Education < 10 years[a]	499 (75.3)	227 (87)
Lower socioeconomic status[a]	384 (57.9)	199 (76.2)
Employed	41 (6.2)	19 (7.3)
Weight of mother at recruitment < 50 kg	362 (57.4)	150 (57.5)
Height of mother < 150 cm	248 (37.5)	111 (42.5)
Parity[a]		
= 1	183 (27.6)	54 (20.7)
≥ 5	45 (6.8)	31 (11.9)
Previous stillbirth (for parity > 1)	69/480 (14.4)	24/207 (11.6)
Hemoglobin < 10 g%	112/532 (21.1)	47/207 (22.7)
Number of antenatal visits < 5[b]	143 (21.6)	70 (26.8)
≥ 2 Tetanus toxoid doses	83 (12.5)	37 (14.2)
HIV status available	307 (46.3)	113 (43.3)
Birthweight ≤ 2,499 g	112/578 (19.4)	44/224 (19.6)
Gestational age ≤ 258 days	112/648 (17.3)	53/255 (20.8)
Stillbirth[a]	18 (2.7)	16 (6.1)

[a] $p < 0.001$.
[b] $p = 0.054$.
Note: SHS, second hand smoke.

urinary infection ($n=4$) were excluded. After further exclusion due to missing information on the outcomes of interest, 924 births were available for the stillbirth analysis, 903 births for gestational age and 802 livebirths for birthweight.

Of the 924 women, 261 (28.2%) either reported smokers in their households or in their workplace (of 60 women that were in paid employment, six reported exposure). Ninety-nine percent of households had one or two smoking members and 1% had three or four. Indoor smoking was reported to be common in 115 households.

The independent samples *t*-test was used to test for differences in mean birthweight and gestational age between exposed and non-exposed groups. Significance of any difference in survival time between exposed and non-exposed groups was evaluated using the Mantel Haenszel chi-squared test (log rank test). The Cox proportional hazards model was used to assess differences in stillbirth rates between exposed and non-exposed groups and adjusted for potential confounders. Days of gestation at birth were used as the timescale. All analyses were conducted using the SPSS statistical software.

Results

There were no differences between the women exposed to SHS and those who were not exposed with respect to maternal age, weight, height, history of stillbirth, the number of TT doses, HIV status availability or the presence of anemia. The exposed women were more likely to be less educated, have lower socioeconomic status, a higher parity and had fewer than five antenatal visits.

Although infants of exposed women were on average 10.6 g lighter at birth than those of non-exposed women, that difference was not significant. The analysis of the data for gestational age also indicated no significant differences between the two groups (Table 1).

The stillbirth rate was, however, significantly higher in the exposed compared with non-exposed group ($p=0.01$) (Table 1). The data also showed evidence of a non-random difference in survival times between the exposed and non-exposed groups (Mantel Haenszel chi-squared $=5.8$, $p=0.016$). The univariable Cox proportional hazards model yielded an unadjusted hazard ratio (HR) of 2.2 (95% CI 1.1–4.4) (Figure 1). After adjusting for education, socioeconomic status, parity and antenatal care, the HR remained almost unchanged at 2.1 (95% CI: 1.1–4.3). As the educational status of the respondent and the family socioeconomic status were not highly correlated ($r=0.3$), both factors were included in the model. HRs were approximately similar among women who reported frequent indoor smoking practices ($n=115$, HR $=2.2$, 95% CI 0.94–5.4) and women

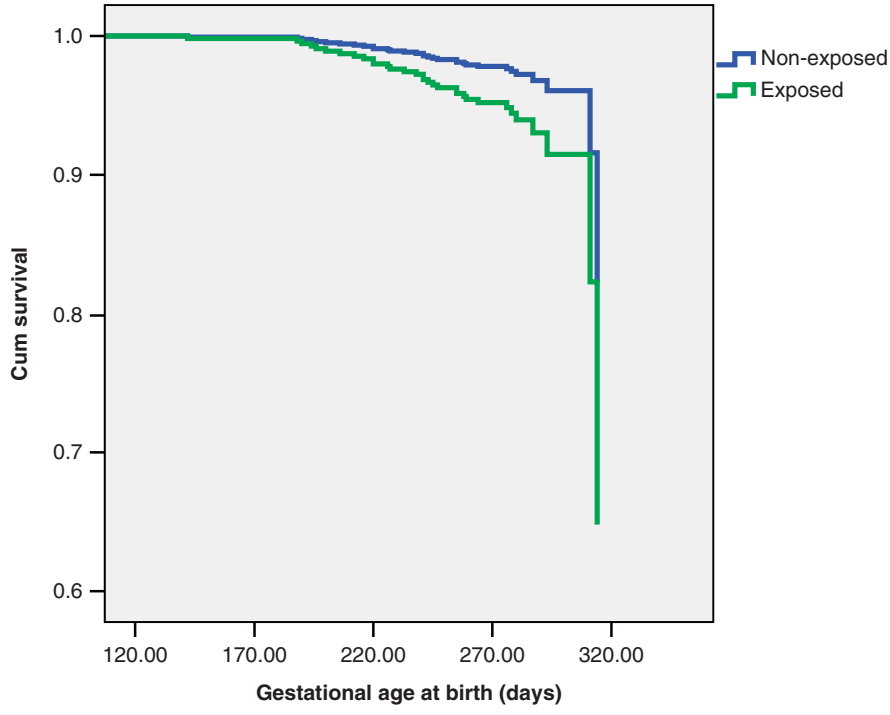

Figure 1. Cumulative survival of the fetus in SHS exposed and non-exposed women. Note: SHS, second hand smoke.

who did not report common indoor smoking ($n=146$, HR=2.2, 95% CI 0.998–4.96).

Discussion

Exposure to SHS was associated with a significant increase in the risk of stillbirth, however, not of low birthweight or preterm delivery. The two-fold higher risk for stillbirth remained unchanged after controlling for potential cofounders (education of mother, socioeconomic status, parity, number of antenatal visits).

The increased stillbirth risk with SHS exposure is supported by the already well-established epidemiological associations between maternal active smoking and stillbirth (1). Direct cigarette smoking and SHS exposure have also been shown to carry a higher risk for the Sudden Infant Death Syndrome (1,8). The biological mechanisms behind the effects for these associations include altered cardio-respiratory responses to hypoxia (13,14), disruption of the timing or intensity of brain cell replication and synapse development related to vital brainstem functions (15,16). These mechanisms or variants of these may also be involved in the relationship between SHS and stillbirth.

Although the difference in birthweight was statistically not significant, it is interesting that the difference was comparable in magnitude to that found in pooled meta-analyses of previous studies undertaken mostly in resource rich countries. Although it is possible that failure to reach significance may be a sample size issue, it is also possible that the dose of exposure to SHS in Mumbai women may be much lower compared with women from high income countries who, in general, are mostly exposed to cigarette smoke. In contrast, the consumption of smoking in India is a mix of cigarettes and bidi use. On average, a male smoker in Mumbai smokes about 15 bidis or about 10 cigarettes per day (17).

Although genetic susceptibility for increased poor health outcomes may be a possible explanation for the high risk for stillbirth in Indian women (18–20), it is more likely that the increased risk for adverse pregnancy outcomes in lower and middle income Indians is the result of cumulative stresses from environmental and social factors including high exposure to SHS (21). Even in high income countries with state-of-the-art medical care, disadvantaged women have higher risks of neonatal death associated with cigarette smoking. The 1980 report of the Surgeon General states that the risk of mortality 'increases directly with increasing levels of smoking during pregnancy' and that the effect is greater in women with other risk factors.

Recurrent exposure to SHS can possibly lead to progressively severe damage to vital organs including the brain (13), liver, kidney and bones (22,23). Many of the toxic chemicals in cigarette smoke, including nicotine (24), carbon monoxide, lead (14) and polycyclic aromatic hydrocarbons (25) that alter vital physiological development, function and birthweight (25,26), are present in higher concentrations in sidestream smoke than in mainstream smoke inhaled by the smoker. Many of these constituents are known to cross the placenta (27); nicotine is particularly toxic (24) and accumulates to a somewhat greater concentration in fetal than in maternal compartments (27).

While maternal active smoking is under the scanner, unrestricted smoking by household members, which is often not directly apparent, can undermine the efficacy of antenatal care programs, particularly for disadvantaged women. This is especially important in societies where patriarchal norms make it difficult for a woman to disagree with her husband on smoking indoors, and exposure at home is more common than at work, as many women are not working outside home. Public health messages and action should target not only any form of tobacco use by the mother, but also to discourage fathers and other members in the household from smoking. These messages will ultimately be of benefit to not only the non-smoking mothers and their babies but also to the smokers as well.

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