Original Article

PASSIVE SMOKING AND RISK OF LEUKEMIA AMONG CHILDREN: A CASE-CONTROL STUDY

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ABSTRACT

Background: Passive smoking is a significant public health concern, particularly in developing countries. This study aimed to investigate the association between passive smoking exposure and childhood leukemia in Bangladesh.

Methods: A case-control study was conducted with 80 histopathologically confirmed leukemia cases and 80 age-matched controls from three tertiary hospitals in Dhaka, Bangladesh. This case-control study was conducted among 160 participants (80 cases and 80 controls) from July 2019 to December 2019. Data were collected through face-to-face interviews and medical record reviews. Binary logistic regression analysis was performed to assess the association between passive smoking and childhood leukemia.

Results: The median (IQR) age of cases was higher [8.0(4-12) years] than that of controls [6.0(9.5) years] and the majority of both groups (66.3% cases and 61.3% controls) were in the age group 1–10 years. Both groups had an equal gender distribution (62.5% male, 37.5% female). The prevalence of passive smoking exposure was higher among cases (82.5%) than in controls (55.0%). Children exposed to passive smoking had significantly higher odds of developing leukemia compared to those not exposed (AOR: 3.57, 95% CI: 1.65-7.72, p=0.001). Higher family income was also associated with increased odds of leukemia (AOR: 2.43, 95% CI: 1.16-5.10, p=0.019). More cases reported indoor exposure to passive smoking compared to controls (56.1% vs 84.1%, p=0.002). Maternal pesticide exposure during pregnancy was higher in cases than controls (25.0% vs 12.5%, p=0.043).

Conclusion: Passive smoking exposure is significantly associated with childhood leukemia in Bangladesh. The study recommends strengthening tobacco control policies and interventions with special attention to passive smoking exposure among children.

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INTRODUCTION

Leukemia is one of the most fatal diseases affecting children worldwide, with increasing morbidity and mortality rates. It is defined as cancer of the blood cells, arising from mutations in blood stem cells during hematopoiesis.[1] Leukemia accounts for about 1 out of 3 cancers in children, with approximately 3,250 children diagnosed annually in the United States alone.[2]

The global prevalence of leukemia has shown a rapid increase over the years. In the United States, although survival rates for children with acute lymphoblastic leukemia (ALL) have improved to approximately 80%, incidence rates have increased by 0.5% annually from 1973 to 1998.[3] The overall incidence of childhood leukemia is about 31% of all cancers in children under 15 years in the USA.[4] Internationally, there is a four-fold variation in age-adjusted incidence rates, with the highest rates observed in Hispanic populations in Costa Rica and Los Angeles.[5] In South-East Asia, leukemia is common among hematological malignancies, with relative proportions varying between 25-40%. In Bangladesh, leukemia was the second most common childhood malignancy (18%) from 2011-2014. A hospital-based study in Bangladesh revealed that acute myeloid leukemia (AML) was the most frequent hematological malignancy at 28.3%, followed by chronic myeloid leukemia (CML) at 18.2%, ALL at 14.1%, and chronic lymphocytic leukemia (CLL) at 3.7%.[6]

Tobacco use, including passive smoking, has been identified as a significant risk factor for various cancers, including leukemia. Tobacco smoke contains more than 60 known human or animal carcinogens, with some substances having an affinity for pluripotent hematopoietic stem cells.[7] Passive smoke exposure, also known as environmental tobacco smoke (ETS) or second-hand smoke, has been causally linked to premature death and disease in children and non-smoking adults.[8] The harmful effects of passive smoke have been recorded since 1928, with scientific interest expanding in the 1970s.[9] Second-hand smoke causes 600,000 premature deaths per year, with more than 4,000 chemicals in tobacco smoke, of which at least 250 are known to be harmful and more than 50 are known to cause cancer.[10]

Globally, The proportion of children younger than 15 years of age exposed to passive smoking in the home ranged from 4.5% (Panama) to 79.0% (Indonesia).[11] In the South-East Asia region, the prevalence of passive smoke exposure is particularly high. A study using Global Adult Tobacco Survey (GATS) data from 21 countries found that approximately 507.74 million children younger than 15 years were exposed to passive smoke at home, with China, India, Bangladesh, Indonesia, and the Philippines accounting for almost 84.6% of the exposed children.[11] In Bangladesh, tobacco consumption is a significant public health issue. A WHO study shows that 20 million people in Bangladesh use tobacco in some form, including 5 million women and 57,000 people die every year due to tobacco-related diseases.[12] Passive smoking is particularly concerning in Bangladesh due to its high population density, lower levels of knowledge and awareness, and lack of strict public law enforcement.

Despite the growing evidence linking passive smoking to childhood leukemia, comprehensive research on this association in developing countries, where the consequences are severe, lags behind. Given the significant public health implications and the lack of comprehensive studies in Bangladesh, there is a critical need to investigate the association between passive smoking and childhood leukemia in the country. This study aimed to address this gap by examining the relationship between passive smoking exposure and childhood leukemia.

METHODS

Study Design, Place, and Population

A case-control study was conducted at three tertiary hospitals in Dhaka, Bangladesh: National Institute of Cancer Research & Hospital (NICRH), Bangabandhu Sheikh Mujib Medical University (BSMMU), and Dhaka Medical College Hospital (DMCH). The study population comprised children aged <1 year to below 18 years attending the outpatient and inpatient departments of these hospitals between January 2019 and December 2019.

Case and Control Selection

Cases were defined as children diagnosed with leukemia, confirmed histopathologically at the study hospitals during the study period. Controls were age-matched (±5 years) children without a history of leukemia, selected from the same institutions. Both cases and controls were selected using purposive sampling technique. Children with secondary neoplasms, those severely ill or mentally unstable, and those whose parents refused to provide informed written consent were excluded from the study.

Sample Size

The sample size was calculated using the formula for case-control studies, resulting in 105 cases and 105 controls. However, due to time constraints, a total of 160 participants (80 cases and 80 controls) were included in the study.

Data Collection Instrument and Technique

Data were collected using a pre-tested semi-structured questionnaire and a checklist. Face-to-face interviews were conducted with parents or guardians to gather information on socio-demographic characteristics, exposure to passive smoking, and other potential risk factors. Medical records were reviewed to collect information on the type of leukemia, child's medical history, and mother's reproductive history.

Data Analysis

Data were analyzed using SPSS version 25. Descriptive statistics, chi-square tests, independent t-tests, and one-way ANOVA were performed to compare characteristics between cases and controls. Pearson's correlation was used to assess the strength and direction of passive smoking exposure. Binary logistic regression was employed to calculate crude and adjusted odds ratios (ORs) with 95% confidence intervals (CIs).

Ethical Considerations

The study was approved by the Institutional Review Board (IRB) of the National Institute of Preventive and Social Medicine (Memo no.: NIPSOM/IRB/2019/111). Written permissions were obtained from the authorities of NICRH, BSMMU, and DMCH. Informed written consent was obtained from parents or guardians of all participants. Privacy and confidentiality were maintained throughout the data collection and analysis process. Anonymity was ensured by not recording names or phone numbers of the respondents.

RESULTS

The median (IQR) age of cases was higher than that of control (8.00 [4-12] vs 6.00 [3 – 9.5]) years, p=0.024). Most participants were in the 1-10-year age group and male (62.5% in both groups). There was a significant difference in education levels between cases and controls (p=0.027), with more cases in secondary education. The median monthly family income was significantly higher for cases (20000 vs 15000 BDT, p=0.024). More cases (76.3%) belonged to the higher income group (≥15000 BDT) compared to controls (58.8%, p=0.028). No significant differences were observed in residence or parental occupation (Table 1).

Table 1. Sociodemographic profile of the participants

Attribute	Case	Control	p-value*
	n (%)	n (%)	
Age (years), Median (IQR)	8.00 (4 – 12)	6.00 (3 – 9.5)	0.024
Age groups			
1 – 10	53 (66.3)	49 (61.3)	0.511
11 – 16	27 (33.8)	31 (38.8)	
Sex			
Male	50 (62.5)	50 (62.5)	1.000
Female	30 (37.5)	30 (37.5)	
Education			
Pre-school	26 (32.5)	34 (42.5)	0.027
Primary	33 (41.3)	38 (47.5)	
Secondary	21 (26.3)	8 (10.0)	
Occupation			
Student	72 (90.0)	70 (87.5)	0.617
Others	8 (10.0)	10 (12.5)	
Monthly Family Income, Median (IQR)	20000 (15000 – 25000)	15000 (10000 – 20000)	0.024
Income groups			
< 15000 BDT	19 (23.8)	33 (41.3)	0.028
≥ 15000 BDT	61 (76.3)	47 (58.8)	
Residence			
Urban	15 (18.8)	10 (12.5)	0.465
Peri-urban	44 (55.0)	44 (55.0)	
Rural	21 (26.3)	26 (32.5)	
Father's occupation			
Businessman	27 (33.8)	25 (31.3)	0.213
Job holders	48 (60.0)	42 (52.5)	
Day laborer	2 (2.5)	8 (10.0)	
Farmer	3 (3.8)	5 (6.3)	
Mother's occupation			
Housewife	73 (91.3)	67 (83.8)	0.284
Businesswomen	2 (2.5)	2 (2.5)	
Sere vice holder	5 (6.3)	11 (13.8)	

*p-value was determined by Chi-square test, Fisher's exact test, independent sample t test and Mann-Whitney U test as appropriate

Significantly more cases were exposed to passive smoking compared to controls (82.5% vs 55.0%, p<0.001). Among those exposed, more controls reported indoor exposure (84.1% vs 56.1%, p=0.002). There was no significant difference in the duration of exposure. Most participants in both groups reported outdoor exposure to passive smoking. Cases were significantly more likely to be exposed to pesticides (56.3% vs 35.0%, p=0.007). No significant differences were found between case and control in the context of exposure to mobile towers, electric towers, or herbicides (Table 2).

Table 2. Environmental characteristics of the participants

Attribute	Case n (%)	Control n (%)	p-value*
Exposed to passive smoking			
Yes	66 (82.5)	44 (55.0)	<0.001
No	14 (17.5)	36 (45.0)	
Place of passive exposure			

Indoor			
Yes	37 (56.1)	37 (84.1)	0.002
No	29 (43.9)	7 (15.9)	
Duration exposed (years)	7.50 ± 3.06	6.80 ±3.43	0.263
Duration exposed in a day (minutes)	39.86 ±11.39	40.67 ±10.21	0.748
Outdoor			
Yes	65 (98.5)	44 (100.0)	0.412
No	1 (1.5)	0 (0.0)	
Duration exposed (years)	7.08 ±2.91	6.25 ±3.14	0.161
Duration exposed in a day (minutes)	44.23 ±14.47	41.47 ±13.36	0.317
Presence mobile tower around home			
Present	42 (52.5)	37 (46.3)	0.429
Absent	38 (47.5)	43 (53.8)	
Presence of electric tower around home			
Present	54 (67.5)	55 (68.8)	0.865
Absent	26 (32.5)	25 (31.3)	
Exposed to pesticide			
Yes	45 (56.3)	28 (35.0)	0.007
No	35 (43.8)	52 (65.0)	
Exposed to herbicide			
Yes	30 (37.5)	29 (36.3)	0.870
No	50 (62.5)	51 (63.7)	
History of blood transfusion			
Present	7 (8.8)	1 (1.3)	0.064
Absent	73 (91.3)	79 (98.8)	

*p-value was determined by Chi-square test, and independent sample t test as appropriate

More mothers of cases were exposed to pesticides during pregnancy compared to controls (25.0% vs 12.5%, p=0.043). A significant difference was observed in family history of leukemia, with 8.8% of cases reporting a family history compared to none in the control group (p=0.014). No significant differences were found for maternal exposure to radiation or herbicides during pregnancy, infertility history, or miscarriage history (Table 3).

Table 3. Other Risk factors associated with leukemia

Attribute	**Case**	**Control**	**p-value**
	n (%)	n (%)	
Exposed to radiation during pregnancy			
Yes	67 (83.8)	61 (76.3)	0.236
No	13 (16.3)	19 (23.8)	
Exposed to pesticide during pregnancy			
Yes	20 (25.0)	10 (12.5)	0.043
No	60 (75.0)	70 (87.5)	
Exposed to herbicide during pregnancy			
Yes	24 (30.0)	16 (21.3)	0.205
No	56 (70.0)	64 (80.0)	
Infertility history			
Yes	1 (50.0)	1 (50.0)	1.000
No	79 (50.0)	79 (50.0)	
Miscarriage history			
Yes	24 (61.5)	15 (38.5)	0.097
No	56 (46.3)	65 (53.7)	
Family history of leukemia			
Yes	7 (8.8)	0 (0.0)	0.014
No	73 (91.3)	79 (100.0)	

*p-value was determined by Chi-square test and Fisher's exact test as appropriate

Binary logistic regression analysis revealed that exposure to passive smoking was significantly associated with increased odds of acute leukemia (adjusted OR: 3.57, 95% CI: 1.65-7.72, p=0.001). Higher family income (≥15000 BDT) was also associated with increased odds of leukemia (adjusted OR: 2.43, 95% CI: 1.16-5.10, p=0.019). While child and maternal exposure to pesticides and family history of leukemia showed increased odds in the crude analysis, these associations were not statistically significant after adjustment for other factors.

Table 4. Binary logistic regression to explore factors associated with acute leukemia among children

Variable	Crude OR (95%CI)	p-value	Adjusted OR (95%CI)	p-value
Exposed to passive smoking				
No	-	-	**-**	**-**
Yes	3.76 (1.84 – 7.70)	**<0.001**	3.57 (1.65 – 7.72)	**0.001**
Monthly family income (Taka)				
<15000	-	-	-	-
≥15000	2.22 (1.13 – 4.37)	**0.020**	2.43 (1.16 – 5.10)	**0.019**
Child exposed to pesticide				
No	-	-	-	-
Yes	2.36 (1.25 – 4.45)	**0.008**	1.21 (0.55 – 2.64)	0.640
Mother exposed to pesticide during pregnancy				
No	-	-	-	-
Yes	2.33 (1.01 – 5.37)	**0.046**	2.17 (0.79 – 5.96)	0.133
Family history of leukemia				
No	-	-	-	-
Yes	16.42 (0.92 – 292.69)	0.057	9.49 (0.53 – 171.19)	0.127

DISCUSSION

This case-control study investigating the association between passive smoking exposure and childhood leukemia in Bangladesh addresses a critical gap in research within developing countries. Our findings reveal a significant association between passive smoking exposure and increased odds of childhood leukemia, contributing to the growing body of evidence on this important public health issue.

The most notable finding of our study is the strong association between passive smoking exposure and childhood leukemia. After adjusting for confounding factors, children exposed to passive smoking had 3.57 times higher odds of developing leukemia compared to those not exposed (95% CI: 1.65-7.72, p=0.001). This result aligns with previous studies that have suggested a link between passive smoking and leukemia among children.[13] Interestingly, our study also found that a higher family income (≥15000 BDT) was associated with increased odds of leukemia (adjusted OR: 2.43, 95% CI: 1.16-5.10, p=0.019). This finding contradicts the findings of a study conducted in Iran[14] and is similar to a study conducted in Canada.[15] Hence, it warrants further investigation as it may reflect differences in healthcare access, diagnosis rates, or other socioeconomic factors that influence leukemia risk or detection.

While our crude analysis showed increased odds for child and maternal exposure to pesticides and a family history of leukemia, these associations were not statistically significant after adjustment. This suggests that passive smoking may be a more potent risk factor for childhood leukemia in our study population. Our findings are particularly relevant in the context of Bangladesh and other developing countries where tobacco use is prevalent[16], and regulations on smoking in public places may be less stringent. The high prevalence of passive smoking exposure among our study participants (82.5% in cases and 55.0% in controls) underscores the urgency of addressing this public health issue.

These results support previous research indicating that the South-East Asia region has a high prevalence of passive smoke exposure[17]. Given that Bangladesh is one of the countries accounting for a significant proportion of children exposed to passive smoke, our findings have important implications for public health policy and intervention strategies. A key strength of this study is its focus on a developing country context, where research on this topic has been limited. The use of histopathologically confirmed leukemia cases and age-matched controls from the same institutions enhances the reliability of our findings.

However, several limitations should be considered. The relatively small sample size (80 cases and 80 controls) may have limited our ability to detect associations with other potential risk factors. The use of purposive sampling could introduce selection bias, potentially affecting the generalizability of our results. Additionally, recall bias may have influenced the reported exposure to passive smoking, particularly among parents of leukemia cases.

Our findings highlight the need for stronger tobacco control policies and public health interventions to reduce passive smoking exposure, particularly in households with children. Educational programs targeting parents and caregivers about the risks of passive smoking could be an important step in reducing childhood leukemia risk. Future research should aim to investigate the dose-response relationship between passive smoking exposure and childhood leukemia risk, explore the potential interaction between passive smoking and other environmental or genetic risk factors, conduct larger, multi-center studies to increase statistical power and generalizability, and investigate the relationship between socioeconomic status and childhood leukemia risk, given our finding of increased odds associated with higher family income.

CONCLUSION

This study provides evidence of a significant association between passive smoking exposure and childhood leukemia in Bangladesh. These findings underscore the importance of implementing and enforcing comprehensive tobacco control policies to protect children from the harmful effects of passive smoking. By addressing this modifiable risk factor, we may be able to reduce the burden of childhood leukemia in Bangladesh and similar settings. The results of this study contribute to the broader understanding of environmental risk factors for childhood leukemia and emphasize the need for continued research and public health efforts in this area, particularly in developing countries where the burden of both tobacco-use and childhood leukemia is significant.

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