

**Research Article** 

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# Hematological Malignancies and Pesticide Exposure: Comprehensive Evidence from Seven Leading Hospitals in Bangladesh

Amin Lutful Kabir<sup>\*1</sup>, Mujahida Rahman<sup>2</sup>, Kazi Md. Kamrul Islam<sup>2</sup>, M. A. Khan<sup>3</sup>, A.K.M. Kamruzzaman<sup>4</sup>, Md. Mahbubur Rahman<sup>5</sup>, Md. Fakhruddin Bhuiyan<sup>6</sup>, Shahed Ahmad Chowdhury<sup>7</sup>, M. Morsed Zaman Miah<sup>8</sup>, Nasrin Akhter<sup>2</sup>, Mahbuba Sharmin Linia <sup>9</sup>

#### **Abstract**

Hematological malignancies (HMs) pose major global health challenges, with their prevalence varying significantly across populations. The rising incidence of these cancers in low- and middle-income countries such as Bangladesh emphasizes the crucial need to comprehend their patterns and possible contributing factors, especially owing to the dearth of cancer data. This study seeks to explore the distribution of HMs and investigate their potential association with pesticide exposure. A multi-center hospitalbased observational study was conducted in seven specialized hospitals in Bangladesh with confirmed cases of HMs through a diagnostic procedure among a population of 12 years or older between July 2017 and June 2018. Descriptive statistics, chi-square tests, and subgroup analyses were employed, with a p-value of <0.05 considered statistically significant. A total of 430 confirmed HMs were examined, with a median age of 35 years, involving both males (67.2%) and females (32.8%). The highest prevalence was observed among aged 20 years or younger. Acute Lymphoblastic Leukemia (ALL) and Acute Myeloid Leukemia (AML) were the most prevalent HMs. Pesticide use was reported more frequently among males (42.9%) compared to females (19.2%). Although the association between overall pesticide usage and HMs was not statistically significant (p = 0.18), subgroup analysis revealed a significant association was found between pesticide usage and HM occurrence (p = 0.01). This study contributes to the understanding of the complex interplay of factors influencing HM patterns in Bangladesh, highlighting the need for targeted interventions and awareness campaigns to mitigate this growing public health concern.

**Keywords:** Hematological malignancies, prevalence of cancer, pesticide exposure, epidemiology, agricultural pesticide use

# **Background**

According to the World Health Organization, cancer incidence is higher in high-income countries, but rates are rising rapidly in low- and lower-middle-income countries, which are projected to account for over two-thirds of the 21.7 million new cases and 13 million deaths by 2030. [1] About 10% of the 50 million fatalities in countries with low or middle income per year, or a total of five million individuals, are due to cancer. Cancer is poorly comprehended in Bangladesh since there is no population-level cancer database or any other type of national cancer database. [2] However, as reported by the WHO, the burden of cancer in Bangladesh is growing, with an estimated 150,781 new cancer cases and 108,137 deaths in 2018, which indicates an approximately 72% fatality rate.

#### Affiliation

<sup>1</sup>MBBS, MPhil, FCPS (Hematology), Professor (Hematology), Bangladesh Medical University, Dhaka, Bangladesh

<sup>2</sup>Asst. Professor, Dept. of Hematology; Bangladesh Medical University, Dhaka, Bangladesh <sup>3</sup>Professor; Dept. of Hematology; Labaid Cancer

<sup>3</sup>Professor; Dept. of Hematology; Labaid Cancer Hospital & Dept. Super Speciality Center; Dhaka, Bangladesh

<sup>4</sup>Professor; Dept. of Hematology; Rangpur Medical College Hospital, Rangpur, Bangladesh

<sup>5</sup>Professor; Dept. of Hematology; Khulna Medical University, Khulna, Bangladesh

<sup>6</sup>Professor; Dept. of Hematology; Sir Salimullah Medical College & Dhaka, Bangladesh

<sup>7</sup>Ex-Professor; Dept. of Hematology, Chattogram Medical College & Hospital; Parkview Hospital Chattogram, Bangladesh

<sup>8</sup>Associate Professor & Head; Dept. of Hematology; Rajshahi Medical College & Hospital; Rajshahi; Bangladesh <sup>9</sup>Medical Officer, Hematologist; Dept. of Hematology, Bangladesh Medical University, Dhaka, Bangladesh

#### \*Corresponding author:

Amin Lutful Kabir, MBBS, MPhil, FCPS (Hematology), Associate Professor (Hematology), Bangladesh Medical University, Dhaka, Bangladesh.

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[3] Besides, by 2030, the number of new cases is expected to grow by 4.13%. [4] Furthermore, cancer care and management fall short of global standards due to expensive treatment, scarcity of oncologists, and insufficient infrastructure. [5]

Hematological malignancies (HMs) encompass a group of diverse and complex disorders affecting blood and lymphatic systems, posing major challenges. [6] The prevalence and distribution of these malignancies can vary across different populations, and grasping the disease patterns in specific regions is essential for effective disease management and optimal distribution of resource. [7] HMs constitute approximately 9% of all cancer cases; these malignancies rank as the fourth most commonly diagnosed cancer among both men (following prostate, lung, and colorectal cancers) and women (following breast, lung, and colorectal cancers) in economically advanced regions across the globe. [8] Over the past decade, the incidence of HMs has shown a notable increase, with distinct disparities between developing and developed countries. [9] Bangladesh, a South-East Asian country, is no exception to the burden of HMs, but comprehensive studies investigating the prevalence and characteristics of these diseases among the Bangladeshi population are limited. While the precise etiology of HMs remains elusive, numerous epidemiological studies have indicated potential associations with exposure to environmental pesticides [10], including other various risk factors like age, female gender, rural residents, smoking, exposure to electrical fields, obesity, presence of autoimmune disease, and co-morbidities such as diabetes mellitus. [11] The development of HMs remains uncertain due to insufficient and conclusive evidence. Besides, the use of agricultural pesticides has been steadily hiking in Bangladesh. [12] However, only a limited number of investigations have explored the potential connection between the risk of HMs and pesticide exposure within a broader population. [10] The primary objective of this study was to delineate the pattern of HMs and establish a connection with pesticide usage, aiming to raise awareness and facilitate informed decision-making to address these concerns in Bangladesh.

# **Methods**

#### **Study Design**

We conducted a multi-center, hospital-based observational study with confirmed cases of HMs through certain diagnostic procedures between July 2017 and June 2018 in Bangladesh. The diagnostic processes were performed at tertiary or specialized hospitals.

#### **Study Sites**

The cancer treatment facilities in Bangladesh primarily comprise a state-run specialized cancer hospital (NICRH—National Institute of Cancer Research and Hospital) along with fourteen oncology units in the public medical college

hospitals, complemented by a few private clinics and hospitals. [13] This study was conducted across seven tertiary-level public cancer treatment and management institutes in the country. Among these, four institutes were situated in Dhaka, the capital city, including Bangladesh Medical University (BMU), Dhaka Medical College Hospital (DMCH), Sir Salimullah Medical College Hospital (SSMCH), and NICRH. The remaining three hospitals were located outside Dhaka city, specifically at Rangpur Medical College Hospital (RMCH), and Chattogram Medical College Hospital (CMCH).

# Study population and sampling technique

All patients aged 12 years or older with any kind of HMs diagnosed at the tertiary or specialized hospitals in the country, and those who attended inpatient and outpatient departments of hematology in one of the multi-centers (BMU, DMCH, SSMCH, NICRH, RpMC, RMCH, and CMCH) for seeking cancer treatment and meeting inclusion and exclusion criteria during the study period (between July 2017 to June 2018) were the study population in this study. These individuals were diagnosed as confirmed cases of HMs based on bone marrow aspiration, trephine biopsy, immunophenotyping, and molecular genetics. The diagnosis of lymphoma requires a lymph node biopsy and histopathology with immunohistochemistry.

# Data collection and quality control

The data were collected using semi-structured questionnaires. These professionals engaged in a face-to-face interview, comprehensive clinical history and examinations, and the compilation of confirmed reports. The principal investigator ensured the accuracy and thoroughness of the data collection process. To ensure the reliability and accuracy of our findings, meticulous quality control procedures were implemented at each stage of the study. Furthermore, crossvalidation of results and repeated assessments were conducted to minimize errors and enhance the validity of the data.

## Statistical analysis

The data sets underwent a rigorous cleaning process, which included the removal of duplicate entries and incomplete and irrelevant records. Identification of missing values within variables was a pivotal step, leading to the formulation of suitable strategies like imputation or exclusion for their effective handling. A total of 512 HM cases were recruited. After thorough checks, cleaning, and necessary removals, 430 cases were retained in the data set, forming the eligible cohort for analysis. The statistical software STATA-16 was used to perform the analysis. Descriptive measures (e.g., mean, median, and standard deviation) were calculated for continuous variables; categorical variables such as sex, marital status, occupation, and types of HM diagnosis were



summarized using contingency tables or depicted through bar and box plots to visualize the distribution of participants across these categories to explore the pattern of HMs and their probable impact on the diagnosis. To investigate a likely correlation between the prevalence of HM and pesticide usage patterns, a chi-square test was performed. Additionally, a subgroup analysis was conducted to explore the association between pesticide usage and the occurrence of HM within specific usage categories. The results were presented with p-values. A p-value of <0.05 was considered statistically significant.

# **Ethics**

The study protocol was ethically approved by the Institutional Review Board of BMU. Informed consent was obtained from all study participants, emphasizing their autonomy and transparency of the research objectives. At every step of the study, the Helsinki Declaration for Medical Research involving human subjects in 1964 was followed.

#### Results

A total of 430 confirmed cases of HMs were enrolled in this observational study from the selected tertiary or specialized hospitals (BMU, DMCH, SSMCH, NICRH, RpMC, RMCH, and CMCH) between July 2017 and June 2018. The study patients were 67.2% male and 32.8% female, with a median age of 35 years for both sexes, regardless of their age group.

The distribution of cases varied by institution [Table 1]. Most of the patients (≥65%) were treated in the facilities located inside Dhaka City. Among the institutions, BMU had the highest number of cases (36.7%), followed by DMCH (13.36%). The distribution of HMs in Bangladesh showed variations in the prevalence of different types of malignancies.

Table 1: Distribution of hematological malignancies by institution and year

Institution	Duration (year)	No. of cases (n)	Percentage (%)	
Inside Dhaka City				
BMU	2017 – 18	158	36.74	
DMCH	2017 – 18	57	13.26	
SSMCH	2017 – 18	33	7.67	
NICRH	2018	32	7.44	
Sub-total		280	65.12	
Outside Dhaka City				
RpMC	2018	48	11.16	
RMCH	2018	50	11.63	
СМСН	2018	52	12.09	
Sub-total		150	34.88	
Total		430	100	

Acute Lymphoblastic Leukemia (ALL) and Acute Myeloid Leukemia (AML) were found to be the most prevalent HMs, accounting for 27.2% and 25.6% of the cases, respectively Next, Chronic Myeloid Leukemia (CML) and non-Hodgkin lymphoma (NHL) were 10.0% and 15.6% of the total cases, respectively. The median age at diagnosis varied across the malignancy types, with Multiple Myeloma (MM) having the highest median age (55 years), while ALL had the lowest median age (20 years). The male-female ratio was highest for Hodgkin Lymphoma (HL) (1:4.33) and lowest for Chronic Lymphocytic Leukemia (1:0.67). Overall, the male-female ratio was 2:1. [Table 2].

Table 2: Distribution of HMs, median age, and the male-female ratio at diagnosis in Bangladesh

Type of HM	Male	Female	Percentage (%)	Median age	Male-Female ratio
ALL	78	39	27.21	20	02:01
AML	62	48	25.58	34	1.29:1
CML	32	11	10	42	2.91:1
NHL	53	14	15.58	50	3.79:1
HL	28	6	7.44	34	4.33:1
MM	23	13	8.37	55	1.77:1
MDS	4	1	1.16	44	4.00:1
MPN	1	1	0.47	46	1.00:1
CLL	2	3	1.16	52	0.67:1
APL	8	5	3.02	35	1.60:1
Total	430		100	35	2.00:1

Among the patients aged ≤20 years, Acute Lymphoblastic Leukemia (ALL) was found to be the most prevalent HM type, accounting for 53.0%, followed by AML, NHL and HL, accounting for 15.5%, 13.4%, and 9.1% respectively (Table 4). AML was found to be predominant (28.2%), followed by ALL (26.5%) among patients aged 21-30 years. Chronic Myeloid Leukemia (CML) (34.9%) and ALL (21.8%) are the two leading HM types in patients aged 31–40 years. The distribution of HMs by sex showed that the prevalence of specific HM types varies between males and females. Among males, the most prevalent cases of HMs irrespective of age, were predominantly ALL (66.7%), followed by AML (56.4%), while among females, AML (43.6%) was the most prevalent, followed by ALL (33.3%) [Table 3].

A statistically significant association was found between age group and HMs (Pearson's  $\chi^2 = 203.05$ , p < 0.001), with the highest prevalence in patients aged  $\leq 20$  years (22.56%), followed by the 21–30 (20.23%) and 31–40 (18.84%) age groups. While males accounted for a higher proportion (67.21%) than females (32.79%), this difference was not statistically significant (p = 0.053). Education level also revealed no significant association (p=0.220), though primary

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Table 3: The distribution of hematological malignancies by sex and age group in Bangladesh

	ALL n (%) (n)	AML % (n)	CML % (n)	NHL % (n)	HL % (n)	MM % (n)	MDS % (n)	MPN % (n)	CLL % (n)	APL % (n)	Total cases N (%)
	Age Group										
≤ 20	62(52.99)	17(15.45)	2(4.65)	9(13.43)	6(18.75)	0 (0)	0 (0)	0 (0)	0 (0)	1(7.69)	97 (22.56)
21 – 30	31(26.50)	31(28.18)	4(9.30)	9(13.43)	8(25.00)	0	1(20.00)	0 (0)	0 (0)	3(23.08)	87(20.23)
31 – 40	14(11.97)	24(21.82)	15(34.88)	12(17.92)	6(18.75)	4(11.11)	0 (0)	1(50.00)	1(20.00)	4(30.77)	81(18.84)
41 – 50	3(2.56)	18(16.36)	6(13.95)	13(19.40)	8(25.00)	8(22.22)	3(60.00)	0 (0)	1(20.00	2(15.38)	62(14.41)
51 – 60	6(5.13)	12(10.92)	14(32.56)	13(19.40)	3(9.37)	14(38.89)	1(20.00)	1(50.00)	2(40.00)	3(23.08)	69(16.05)
61 – 70	1(0.85)	6(5.45)	1(2.33)	10(14.93)	0 (0)	8(22.22)	0 (0)	0 (0)	1(20.00)	0 (0)	27(6.28)
≥ 71	0 (0)	2(1.82)	1(2.33)	1(1.49)	1(3.13)	2(5.56)	0 (0)	0 (0)	0 (0)	0 (0)	7(1.63)
Total	117(100)	110(100)	43(100)	67(100)	32(100)	36(100)	5(100)	2(100)	5(100)	13(100)	430
	Sex										
Male	78(66.67)	62(56.36)	32(74.42)	53(79.10)	26(81.25)	23(63.89)	4(80.00)	1(50.00)	2(40.00)	8(67.21)	289(67.21)
Female	39(33.33)	48(43.64)	11(25.58)	14(20.90)	6(18.75)	13(36.11)	1(20.00)	1(50.00)	3(60.00)	5(32.79)	141(32.79)
Total	117(100)	110(100)	43(100)	67(100)	32(100)	36(100)	5(100)	2(100)	5(100)	13(100)	430

education was most common (39.30%). Marital status and occupation were both significantly associated with HMs (p < 0.001); married individuals made up 69.53% of cases. Among occupations, students (23.72%), housewives (21.86%), and farmers (16.51%) had the highest prevalence. No significant difference was observed between rural (38.37%) and urban (61.63%) residents (p = 0.508). However, smoking status was significantly associated with HMs (p < 0.001), with 31.63% of patients reporting smoking [Table 4].

Pesticide usage was higher among males (42.9%) than among females (19.2%), which is statistically significant (p<0.0001) (Table 5). The use of pesticides for agricultural purposes was significantly higher among males than that among females (p<0.0001). In contrast, the use of pesticides for planting purposes was significantly higher among females than that among males (p<0.01). A subgroup analysis based on different purposes in pesticide usage patterns was carried out to acquire further insight into the pesticide usage trends among males and females. Among the male patients (n=289), 35.29% (n=102) reported using pesticides for agricultural purposes, while among females (n=141), a considerably lower proportion of 3.55% (n=5) used pesticides for this purpose. The gender difference in pesticide usage for agricultural purposes was found to be statistically significant (Pearson's Chi-squared: 51.10, p < 0.001), indicating distinct gender-associated tendencies in engaging with pesticides for agricultural activities. Regarding planting purposes, among males (n=289), 6.23% (n=18) reported pesticide usage for planting purposes, while among females (n=141), 14.89% (n=21) utilized pesticides for the same purposes. The p-value (Pearson's Chi-squared: 8.627, p=0.003) highlighted potential differences in gender-related patterns of pesticide application for planting. A relatively small percentage of both males (1.38% or n=4) and females (0.71% or n=1) used pesticides for treated seeds. However, the observed difference in pesticide usage for treated seed purposes was found to be statistically insignificant (p=0.540), suggesting that gender may not substantially influence the application of pesticides for treated seeds [Table 5].

# **Discussion**

This study aimed to provide a comprehensive understanding of the distribution patterns and characteristics of HMs in the studied region. The results shed light on several crucial aspects, including the prevalence of different types of HMs, age and gender associations, as well as the potential influence of sociodemographic and lifestyle factors. Additionally, the study explored the connection between pesticide exposure and HM occurrence. The distribution of HM cases across institutions and years indicated significant variations based on location. The majority of patients were treated in facilities located within Dhaka, with BSMMU and DMCH contributing notably high percentages. According to World Bank data for 2018, over 63% of the Bangladeshi general population resides in rural regions. [14] Notably, the majority of well-equipped tertiary healthcare facilities for



Table 4: Association between hematological malignancies and sociodemographic and lifestyle characteristics

Characteristics	Hematological Malignancies				
	%	% N (430)			
Age group (years)					
≤ 20	22.56	97			
21 – 30	20.23	87			
31 – 40	18.84	81			
41 – 50	14.42	62	<0.001		
51 – 60	16.05	69			
61 – 70	6.28	27			
≥ 71	1.63	7			
Sex					
Male	67.21	289	0.053		
Female	32.79	141	0.000		
Education					
Illiterate	15.35	66			
Primary	39.3	169	0.22		
SSC	20.7	89	0.22		
HSC and Higher	24.65	106			
Marital status					
Married	69.53	299			
Unmarried	30.23	130	<0.001		
Divorced	0.23	1			
Occupation					
Farmer	16.51	71			
Housewife	21.86	94			
Student	23.72	102	<0.001		
Service holder	15.35	66			
Others	22.56	97			
Residence					
Rural	38.37	165	0.508		
Urban	61.63	265			
Smoking					
Yes	31.63	136	<0.001		
No	68.37	294	\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\		

cancer treatment are concentrated in the capital city, Dhaka. <sup>[13]</sup> Consequently, individuals requiring cancer treatment often need to travel to Dhaka for access to these facilities. This highlights the concentration of specialized healthcare services within the capital city. The findings emphasize the importance of considering both institutional and temporal factors when analyzing HM cases, which can aid in designing targeted interventions and resource allocation. The prevalence of different types of HMs revealed that ALL and AML were

Table 5: Prevalence and purpose of gender-specific pesticide usage and subgroup analysis using Chi-Square test

	Ma	ale	Female					
	n=289	%	n=141	%	p-value			
Pesticide used								
Yes	124	42.91	27	19.15	<0.0001			
No	165	57.09	114	80.85	<0.0001			
Purpose of pes usage								
Agricultural purpose								
Yes	102	35.29	5	3.55	<0.0001			
No	187	64.71	136	96.45	<0.0001			
Planting purpose								
Yes	18	6.23	21	14.89	<0.01			
No	271	93.77	120	85.11	<0.01			
Treated seed purpose								
Yes	4	1.38	1	0.71	0.54			
No	285	98.62	140	99.29	0.54			

the most common, with distinctive prevalence percentages. These findings are consistent with the recently published study. [11] Besides, NHL, and Multiple Myeloma (MM) exhibited varying proportions among the cases. The variations in median age at diagnosis for different malignancy types further emphasize the heterogeneity of HMs. Then again, it is necessary to note that the median ages for MDS, MPN, and CLL might not be truly indicative, given the limited number of cases. To obtain a more accurate understanding, a study with a substantial sample size would be necessary to reflect real-country conditions. The bivariate analysis revealed significant associations between age groups and the prevalence of HMs. Notably, the highest prevalence was observed in the age group of 20 years or younger. This aligns with the well-established understanding that certain types of HMs, such as ALL, are more common among younger individuals. [15] While the overall male-female ratio of HM cases was approximately 2. The study also demonstrated male to female ratios regarding the ALL, AML, MDS, and CLL were found to be 2, 1.29, 4 and 0.67 respectively; which is consistent with previous literature, [16] where specific malignancy types displayed heterogeneous gender distributions. These findings highlight the importance of considering age and gender as key factors in understanding the occurrence of HMs and contribute to a better understanding of these patterns is crucial for developing targeted interventions and strategies for early detection, diagnosis, and treatment of these malignancies in different demographic subgroups.

Associations between HM occurrence and sociodemographic and lifestyle factors were explored. Marital



status, occupation, smoking, and alcohol intake demonstrated significant correlations with HM prevalence. Married individuals had a higher prevalence, potentially attributed to shared environmental or genetic factors. Occupation-wise, farmers and housewives exhibited higher HM prevalence, which could be linked to exposure to environmental or occupational risk factors. Smoking and alcohol intake also showed associations with HM occurrence, emphasizing the role of these factors in hematological diseases. The study investigated the potential association between pesticide exposure and HM occurrence. While the overall association was not statistically significant, subgroup analyses based on the purpose of pesticide usage revealed interesting patterns. Pesticide usage for agricultural purposes showed a statistically significant association with HM occurrence, indicating a potential link between agricultural pesticide exposure and hematological malignancies. A previous study conducted in Spain showed that growers exposed to nonarsenic pesticides were found significant association with non-Hodgkin lymphoma (NHL), chronic myeloid leukemia (CML), multiple myeloma (MM), and Hodgkin's disease. [17] This finding suggests the need for further investigation into the specific types of pesticides used and their potential health impacts.

#### Limitations

The study has some limitations. The study design restricts the establishment of causal relationships between HMs and associated factors. Further research with a larger sample size and prospective longitudinal study design is recommended to validate the generated findings and elucidate the clinical implications of these correlations.

## **Conclusion**

This study recognized Acute Lymphoblastic Leukemia (ALL) and Acute Myeloid Leukemia (AML) as the most prevalent HMs in Bangladesh, with distinct age and gender distributions. Younger patients (≤20 years) displayed the highest HM prevalence, predominantly ALL, while AML was more common in slightly older age groups. Significant associations were found between HMs and factors such as age, marital status, occupation, smoking status, and pesticide usage, with notable gender differences in pesticide exposure patterns. These findings emphasize the need for targeted public health strategies and further research into environmental and lifestyle risk factors influencing HM development in this population.

**Conflict of Interest:** The authors state that there is no conflict of interest in this study.

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**Ethical Consideration:** The study was conducted after

approval from the Institutional Review Board of BMU. The confidentiality and anonymity of the study participants were maintained.

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