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Epidemiological Evaluation of Hematological Malignancies in HIV-Positive Patients at Lady Reading Hospital, Peshawar Pakistan

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ABSTRACT

HIV causes immunodeficiency because of retroviruses; it predisposes a patient to opportunistic infections and malignancy. HMs constitute a major clinical problem for populations infected with HIV, especially in areas where fully developed ART is not accessed. Objective: To evaluate the prevalence and its associated risk factors of HMs in HIV-positive patients at Peshawar's LRH. This was a cross-sectional study involving 289 HIV-positive patients recruited from January 2021 to January 2023. The data were collected on demographic patients, the duration of HIV infection, and the incidence of hematological malignancies. Statistical analyses included association studies between malignancies and age, gender, HIV duration, and body weight. The age range was as follows: mean age was 42.08 ± 9.47 years, and males formed the majority of the study at 84.1%. The hematological malignancies were detected in 2.4% of the cohort. The risk factors significantly correlated with HMs included age, with a frequency of 3.8% in patients aged 41–60 ($p = 0.046$), prolonged HIV infection with >12 months of infection, determined in 7%, $p < 0.001$, and body weight>80 kg, 3.9%, $p = 0.039$. A relevant correlation was not found between gender, $p = 0.905$.

Hematological malignancies are rare and represent an important risk among HIV-infected patients. Age, duration of HIV infection, and greater body weight have

emerged as key risk determinants. These findings underscore the pressing need for targeted cancer surveillance and management strategies in HIV populations, particularly in resource-limited settings.

Keywords: HIV; Hematological Malignancies; Antiretroviral Therapy; Immunodeficiency; Epidemiology of Cancer; Lymphoma.

INTRODUCTION

Human Immunodeficiency Virus (HIV) is a retrovirus that causes acquired immunodeficiency syndrome (AIDS), the most advanced stage of HIV infection when the immune system has been severely impaired. Typically, following an initial acute phase, HIV becomes a chronic infection that may persist for many years, causing progressive impairment of the immune function. If left untreated, AIDS leads to severe opportunistic infections and malignancies; many of these are fatal. Most of the hematological abnormalities such as cytopenia and malignant transformations of hematopoietic cells are a result of direct viral effects, secondary infections, or adverse responses to HIV-related therapies.

Hematological problems are quite common in HIV patients, with anemia occurring in about 80% of these patients, mainly being normochromic normocytic. Leukopenia and thrombocytopenia are also common and can be very variable in their severity. Blood smears usually have abnormalities in morphology but some patients have characteristics of hematologic neoplasms including the kind associated with Burkitt-type acute lymphoblastic leukemia. HIV-infected individuals are still markedly more susceptible to several hematological malignancies, among them KS, NHL, and certain ADCs, like cervical carcinoma. The expansion of ART has dramatically decreased the incidence of these neoplasia: KS rates have decreased by 60-70% and those of NHL, by 30-50%, from the predomination rate. However, this risk of having KS was 800-fold, NHL 10 times, and was still much higher in those who were HIV-positive compared to the general population. Another emerging problem NADC which incidence continues to rise everywhere in the world.

In 2023, it has been estimated that around 39.9 million people were living with HIV, 1.3 million new infections, and 630,000 deaths due to AIDS worldwide. While 30.7 million now benefit from access to ART, there are significant regional gaps in treatment coverage. New infections have declined by 60% since 1995, and AIDS-related deaths have decreased by 69% since 2004. Still, the international targets achieved thus far were not realized, signifying that the management of the disease with its complications is indeed challenging.

In Pakistan, cases of HIV-positive patients have increased more than doubled in the past decade which rose to 97,000 in 2009 and nearly 210,000 by mid-2022. In detail, only 7% of the cases are undergoing ART, leaving the vast majority at heightened risk for HIV-related complications, which include malignancies. Of all these malignancies, lymphomas are the most prominent hematological cancers. A series study from Punjab has reported hematological malignancies in 1.06% of HIV-positive patients. Among all, lymphomas were the most common type of

hematological malignancies. Diffuse large B-cell lymphoma is one of the most common and aggressive hematological malignancies in HIV-infected patients; high incidence rates are observed even with high coverage of ART in many regions of the world.

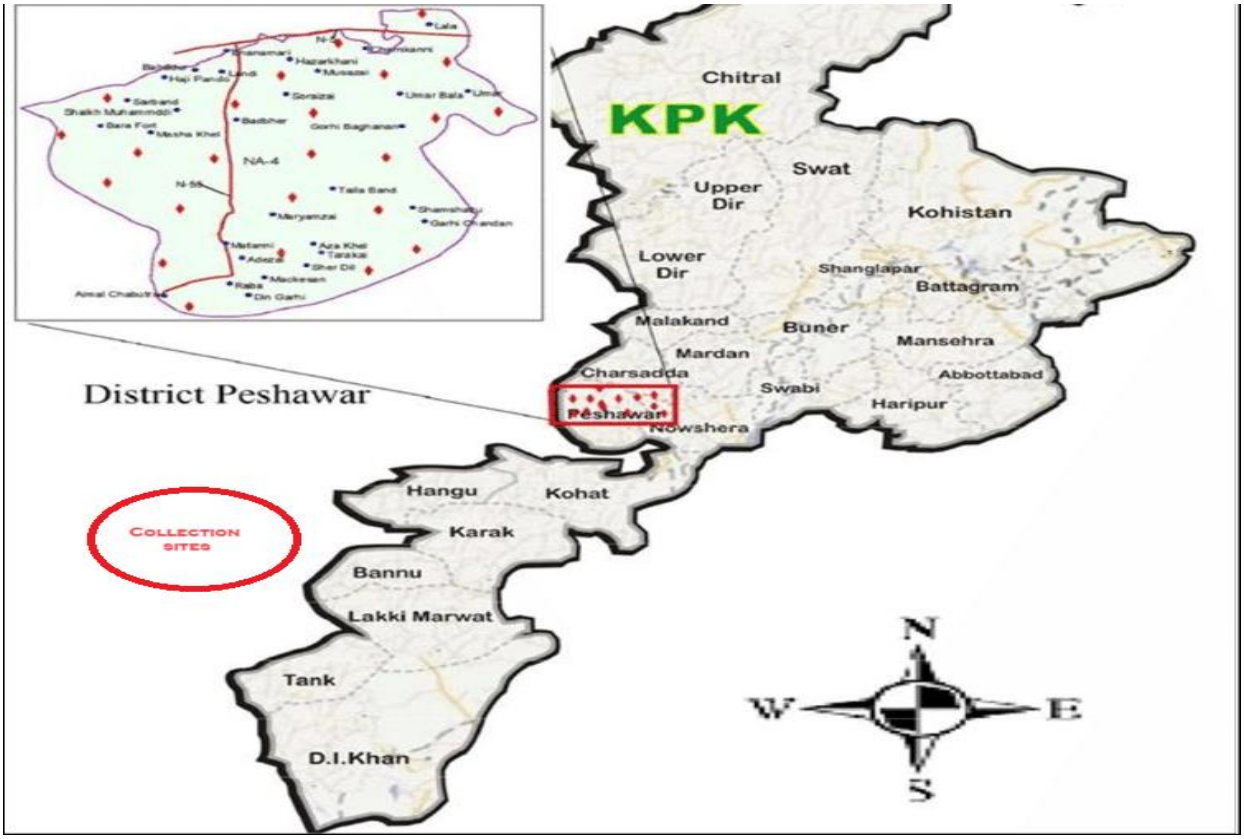
Low CD4 cell counts, prolonged untreated HIV infection, and male gender are risk factors for hematological malignancies in HIV-positive. The situation is compounded by the risk factors in the case of Pakistan where ART is limited to only 10% of the affected population, thus adding another layer of complexity in managing HIV-related malignancies.

Although recent data may show a relatively low overall prevalence of hematological malignancies in HIV-positive groups, the increasing trend of HIV in Pakistan highlights a possible boost in the associated malignancies in the future. Thus, the study aims to fill this critical gap by examining the frequency and risk factors related to hematological malignancies among HIV-positive patients attending Lady Reading Hospital in Peshawar. Elucidation of these patterns will provide more insights into how to optimize the clinical management of such patients and will help in making appropriate resource allocation and developing targeted cancer prevention strategies in HIV-positive populations within a resource-limited environment.

MATERIALS AND METHODS

Study Area Peshawar

The study in District Peshawar, Pakistan, at geographical coordinates 34° 00' 28.80" N, 71° 34' 42.56" E.



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Study Design and Duration

This was a cross-sectional study conducted in the Medicine Department of Lady Reading Hospital, Peshawar for a period of two years from January 2021 to January 2023. This study was aimed at establishing the prevalence of hematological malignancies and potential risk factors among HIV-positive patients who report to the hospital.

Sample Size and Sampling Method

A total of 289 HIV-positive patients participated in the study. The minimum sample size was determined through the use of the WHO sample size calculator, assuming a 95% confidence level, an estimated prevalence of 1.72%, and an absolute precision of 1.5%. A non-probability consecutive sampling technique was employed to involve all eligible patients who fit the qualifications set.

Patient Eligibility

The inclusion criteria included all HIV-positive patients aged between 20 and 60 years with a confirmed diagnosis for more than six months. HIV infection was established by a western blot assay whereby a test was considered positive if there was the presence of at least two bands from the p24, gp41, and gp120/160 bands. Exclusion criteria included any patient who had a history/record of earlier anticancer treatment, females who tested positive through ultrasound confirmation, and those patients unwilling to give their informed consent.

Ethical Approval and Informed Consent

The study was subjected to approval by the ethical committee of the hospital. Furthermore, all the participants were provided with a written informed consent. Their confidentiality was maintained clearly without breach during the studies. Moreover, all risks and benefits associated with this study were clearly communicated to all participants for them to effectively and willingly enroll in the research.

Data collection and Histopathological evaluation

All demographic baseline information such as age, gender, duration of HIV infection, and body weight were recorded. Patients suspected of having lesions or lymphadenopathy underwent surgical excision or incision biopsy of lymph nodes or extra-nodal tissues for histopathological examination within the hospital laboratory to confirm the presence of hematological malignancies.

Data Management and Statistical Analysis

The data were first captured on Microsoft Excel, which was later transferred to SPSS version 25 for detailed analysis. Descriptive statistics: Frequency and percentages of categorical variables, such as gender, and the presence of hematological malignancies, have been calculated for the categorical variable. Quantitative variables: Age, duration of HIV infection, and body weight were summarized as a mean and standard deviation.

Stratification and Risk Factor Analysis

Data was further stratified based on factors like age, gender, duration of HIV infection, and weight to assess the risk factors. It followed correlation analyses between the stratified variables and hematological malignancies employing post-stratification Chi-square tests. The p-value set was ≤ 0.05, and a statistically significant correlation would be considered if the result $p \leq 0.05$. The extent of detailed stratification will help ensure much better analytical and therefore interpretative robustness as well as identification of key demographic and clinical determinants in association with hematological malignancies in HIV-positive patients.

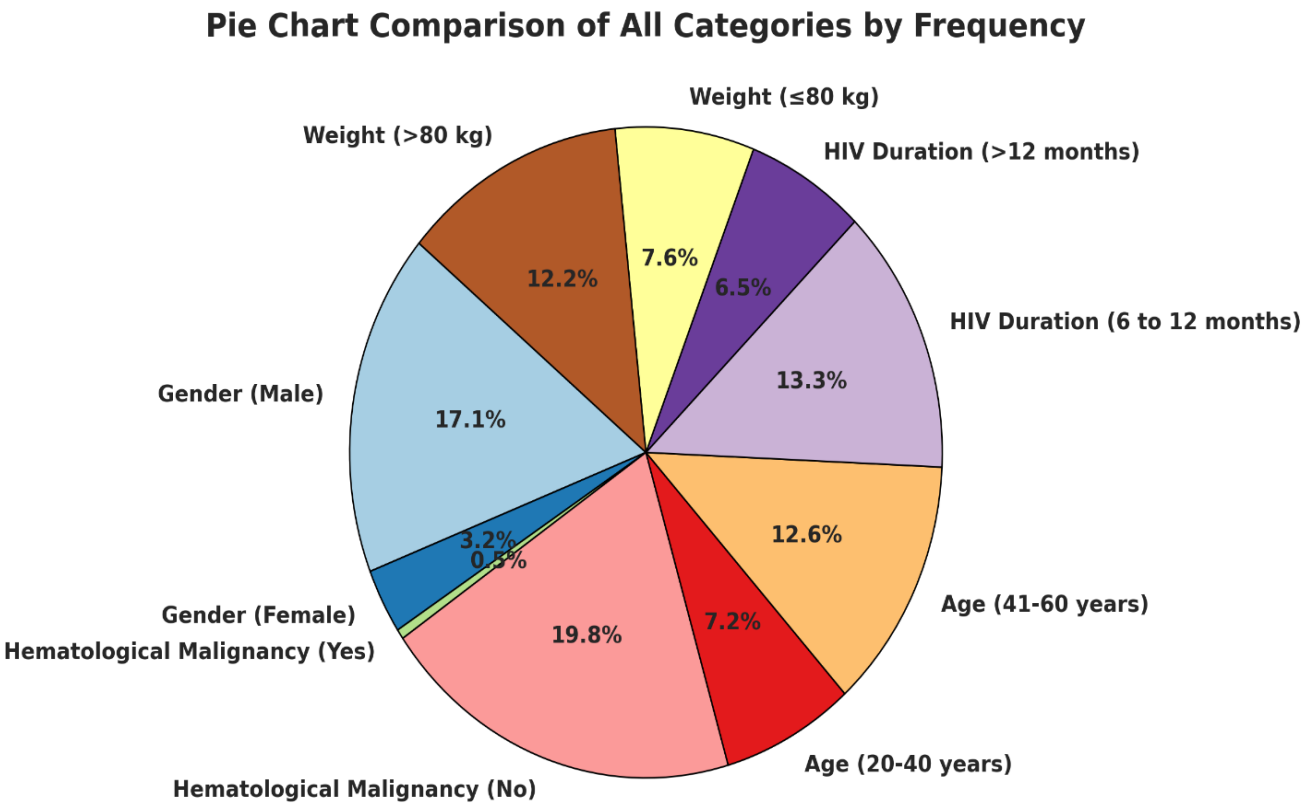

Figure 1: Frequency, Percentage, Hematological Malignancy, and P-values for Different Patient Characteristics

Table 1 Baseline Characteristics and Hematological Malignancy Incidences of HIV affected Patients at LRH Hospital Peshawar

Characteristic	Frequency	Percentage (%)	Hematological Malignancy (%)	p-value
Gender (Male)	243	84.1	2.5%	0.905
Gender (Female)	46	15.9	2.2%	0.905
Hematological Malignancy (Yes)	7	2.4	100%	-
Hematological Malignancy (No)	282	97.6	0%	-
Age (20-40 years)	103	100	0%	0.046
Age (41-60 years)	179	96.2	3.8%	0.046
HIV Duration (6 to 12 months)	189	100	0%	0.000
HIV Duration (>12 months)	93	93	7%	0.000
Weight (≤80 kg)	108	100	0%	0.039
Weight (>80 kg)	174	96.1	3.9%	0.039

This baseline data describes the characteristics and prevalence of hematological malignancies in HIV-positive patients attending the Lady Reading Hospital, Peshawar. A total of 289 patients were included in the study, with an overwhelming male predominance: at 84.1% and females at 15.9%. Hematological malignancies were reported in 2.4% of the cohort; this frequency is relatively low when compared to global averages. There was a marginal difference by gender, as males exhibited a malignancy rate of 2.5% compared with the 2.2% reported in females, and the p-value was 0.905. This means that there is no statistically significant variation in malignancy between genders. Comparison by age exhibited striking differences between the age groups: no malignancies were reported from the 20–40-year age group, whereas 3.8% of individuals in the 41–60-year age group reported malignancy, and the corresponding p-value is 0.046. This trend points to the fact that the majority of the critical risk factor was age itself in HIV patients, who are more at risk of hematological cancers when advanced in age. The length of time the patient was infected with HIV was also one of the major predictors. No patient in the study, who was infected with HIV for 6–12 months had malignancies. However, 7% of them were diagnosed with hematological cancers after an infection time that is more than 12 months, and the p-value was highly significant at 0.000. Extended HIV infection is likely to be associated with greater immunosuppression as well as increased oncogenic potential. Weight was another important predictor. None of the patients with a body weight ≤80 kg had malignancies, whereas 3.9% of those weighing more than 80 kg were diagnosed. Thus, a connection may exist between higher weight and the danger of malignancy, which is made even stronger by the presence of a p-value of 0.039. This could have plausible relations with metabolic syndrome, chronic inflammation, or ART-induced weight gain in heavier patients. In combining the above findings, it indicates that older age is related to a longer duration of infection by HIV, and higher body weight are major determinant in the development of risks for hematological malignancies in the HIV-positive population, thus demanding effective screening and management strategies to combat these risks. These significant associations do indicate that there is a need to continuously monitor infections and implement targeted interventions in resource-poor settings, especially where the management of HIV is still a challenge. Gender does not appear to play a significant role in malignancy risk in this population; however, females are relatively underrepresented in the sample, and this might call for further research using a balanced gender cohort.

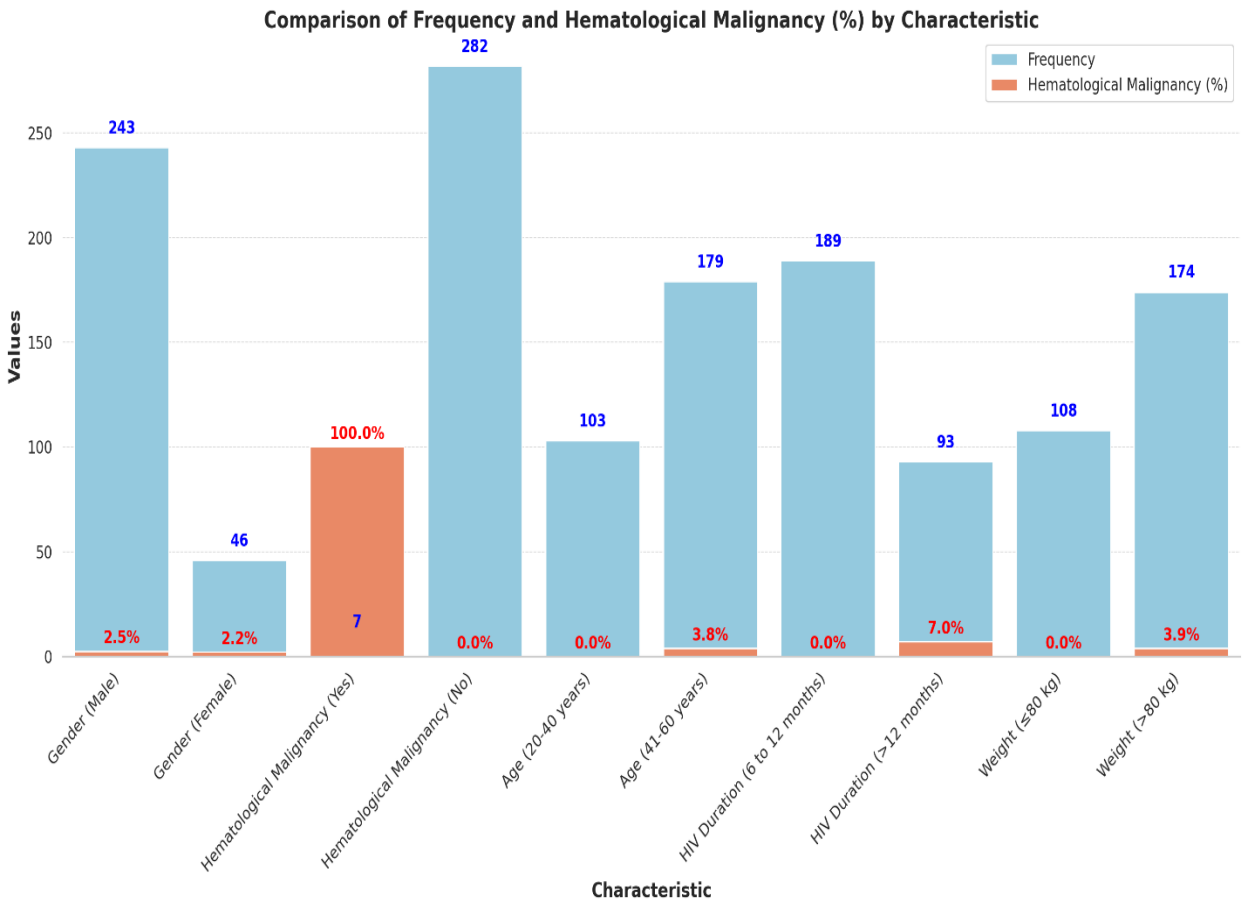

Figure 2: Comparative Analysis of Hematological Malignancy Incidence in Different Patient Categories,

DISCUSSION

Our group has reported a prevalence rate of 2.4% for hematologic malignancies among the HIV patients at Lady Reading Hospital, Peshawar, which is relatively low compared with several reports from international studies. In fact, Mbulaiteye et al. have mentioned a prevalence rate for HMs between 5-10% among untreated HIV-positive cohorts, which was significantly higher than what we have observed. This may be because of differences in populations, HIV management practices, and access to ART. For our population, most persons might have had some provision of ART, not necessarily consistently enough, and this may have contributed to lower prevalence rates of HMs. Indeed, the study on age groups indicated a higher incidence of hematological malignancies among the 41-60 years age group which was significantly different from the 20-40 years age group which had no malignancy cases; ($p = 0.046$). This goes a long way to agree with Shiels et al., who diagnosed that elderly HIV-infected patients are at increased risk for the

emergence of AIDS-defining and non-AIDS-defining cancers as they continue to expose them to the same virus plus associated comorbidities. At the same time, it has been noticed that individuals older than 40 years are at a significantly increased risk for the development of non-Hodgkin lymphomas as compared with their younger counterparts. Thus, age emerges to be one of the major determinants of malignancy-risk within HIV-positive populations.

Duration of HIV was one of the strong predictors of hematological malignancy among our cohorts. We noted a prevalence of 7% among those infected with HIV for more than 12 months, compared to 0% among those diagnosed within 6 to 12 months ($p < 0.001$). This outcome agrees well with Engels et al., who stated that a long duration of HIV infection strongly correlates with increased risks of lymphomas and other HMs, even under ART coverage. Chronic immune activation and inflammation, as well as oncogenic viruses like EBV, may be contributing factors during long-term HIV infection.

Gender did not correlate with hematological malignancy in our study. Males and females matched equally at 2.5% and 2.2%, respectively ($p = 0.905$). This finding is contrasted by that of Biggar et al. which showed notably higher occurrences of lymphomas in HIV-positive men than in women. These differences may stem from gender-specific mechanisms of immune response and behavioral risk factors. Our sample likely had a relatively low proportion of female participants (15.9%), further reducing the power to identify gender-based differences. Socio-cultural factors in Pakistan may also lead to gender-specific differences in the presentation and diagnosis of HIV and malignancies in comparison to Western settings.

Body weight of ≥80 kg was associated with a higher incidence of HMs at 3.9%, compared to 0% in those weighing ≤80 kg ($p = 0.039$). This finding is somewhat surprising since most previous studies have associated lower body weight and malnutrition with poor outcomes in HIV-positive patients. However, Crum-Cianflone et al. suggested that an increased risk of cancer with a higher BMI could be attributed to metabolic syndrome, ART-related adiposity, and chronic inflammation. In our low-resource setting, nutritional patterns are distinctly different from the high-resource environments. The association of weight with risk for malignancy could be an indicator of particular local factors that require further research.

Comparing our findings with the other low-resource areas, the overall prevalence of HMs in our study is still relatively low. For example, one study from sub-Saharan Africa has shown the prevalence of 4-6% of hematological malignancies among ART-naive HIV-positive persons. This is more likely due to over-immunization

and lower utilization of ART, contrary to our partial ART coverage in our setting. In another study, Park et al. reported that lymphomas accounted for more than 50% of all malignancies reported among African HIV-positive patients. Again, this relates to our observation about the predominant nature of lymphomas in the HM observed in our cohort.

The critical difference between our study and the existing literature might be within the local healthcare context, access to ART, and HIV case management strategies. We did, however, find a modestly lower incidence of HMs in our cohort, which may be indicative of improvements in accessibility of ART-even though ART coverage is still suboptimal in Pakistan at only 10-15% of the HIV-positive population. Our findings stress an important requirement for focused interventions for cancer prevention among HIV-infected patients, with particular emphasis in resource-limited settings where access to ART remains limited.

Conclusion: Our results show a generally lower overall prevalence of hematological malignancies than reports internationally, but the associations with age, duration of HIV infection, and body weight are consistent with the general research conducted around the world. These findings therefore suggest that partial access to ART is insufficient to mitigate the risks associated with HM since demographic and clinical factors continue to remain determinants of the risk of HM among HIV-infected individuals. Such future research may focus on larger multicentric studies to validate these associations, and even identify more risk factors specific to low-resource settings.

Author Contributions:

Muhammad Nisar conceptualized the study, developed the methodology, curated the data, and prepared the original draft. **Nisar Ahmad** contributed to formal analysis, investigation, data interpretation, and visualization. **Asad Ullah** was responsible for data collection, software implementation, validation, and review and editing of the manuscript. **Saeed Ullah** managed project administration, resources, supervision, and funding acquisition. **Muhammad Waqar Farooqi** provided support in data analysis, manuscript drafting, and overall coordination. **Fawad Khan** performed critical revisions, reviewed and edited the manuscript, and provided final approval.

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