

Transmission Patterns and Risk Factors for Hematologic Neoplasms in HIV-Exposed Mothers and Infants

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Abstract

This study explores the prevalence and risk factors of hematologic neoplasms in HIV-exposed pediatric patients (infants and children) and their mothers in the context of vertical transmission. A total of 100 HIV-affected individuals were included, with a focus on both gender and age-based prevalence patterns. The study also examined how HIV duration, nutritional status, ART adherence, viral load, and CD4 count contribute to the development of hematologic neoplasms. The results show that male infants exhibited a higher frequency of hematologic neoplasms compared to females, with increasing

prevalence across age groups—particularly in 6–10 and 11–16 years. Mothers had a 100% frequency of being HIV-infected, with a 2.8% prevalence of neoplasms. Furthermore, longer HIV duration (>1 year) and high viral load were associated with significantly higher neoplasm rates. Nutritional deficits, including malnutrition, significantly increased the risk of developing hematologic neoplasms. Poor ART adherence was linked to a higher prevalence compared to good adherence. Vertical transmission of HIV from mother to infant was identified as a major risk factor, with a 3.5% prevalence of neoplasms among vertically transmitted infants. These findings underline the critical role of early diagnosis, ART adherence, and nutritional management in reducing the risk of hematologic complications in HIV-affected children and their mothers.

INTRODUCTION

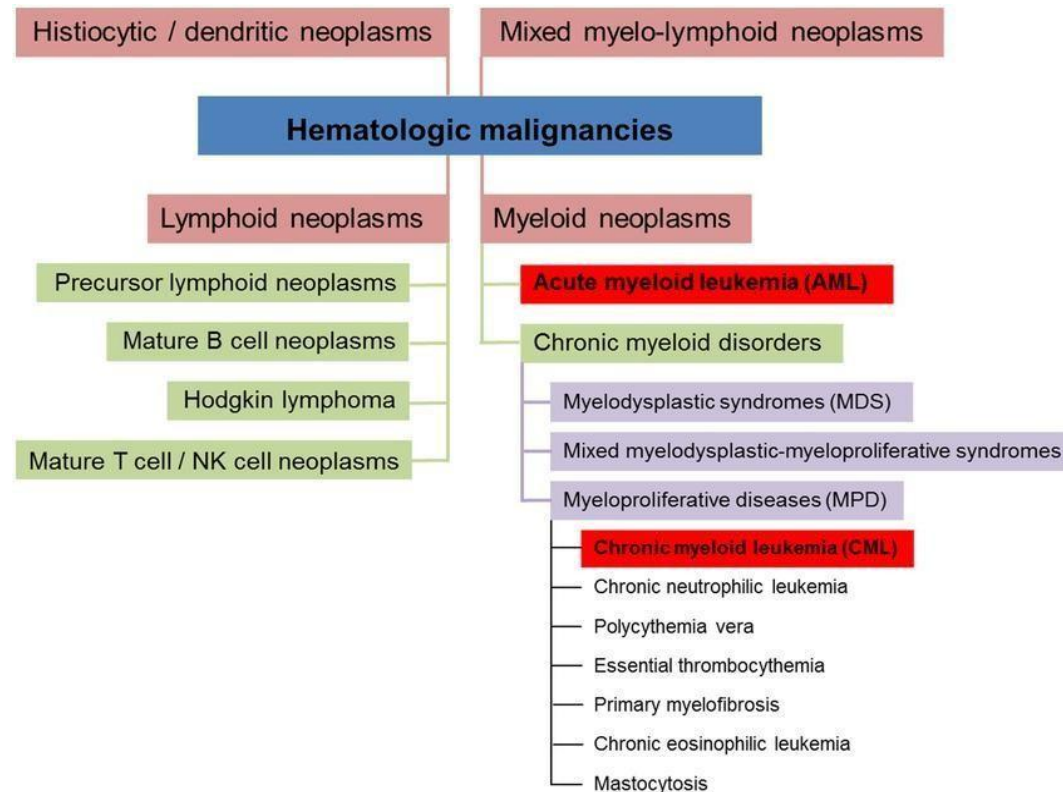
Human Immunodeficiency Virus (HIV) is a retrovirus that attacks the immune system, specifically targeting CD4 T cells, which are crucial in protecting the body from infections and diseases. The progression of HIV leads to acquired immunodeficiency syndrome (AIDS), which marks the most severe phase of the infection, characterized by profound immune suppression and increased susceptibility to opportunistic infections and cancers. Among the many complications associated with HIV, hematologic malignancies (HMs) represent a significant cause of morbidity and mortality (Bhatt et al., 2020). These malignancies, including non-Hodgkin lymphoma (NHL), Kaposi's sarcoma (KS), and other hematologic neoplasms (HNs), are particularly common in HIV-infected individuals due to the virus's impact on immune function. The advent of antiretroviral therapy (ART) has significantly improved the prognosis of HIV-positive patients by suppressing the virus and restoring immune function. ART has been associated with a decrease in the incidence of several types of cancer, including hematologic malignancies (Gavalda et al., 2017).

However, despite these advancements, the risk of developing hematologic malignancies remains elevated among individuals with HIV, especially in resource-limited settings where ART access is limited. In countries like Pakistan, where healthcare infrastructure is often inadequate and ART availability is restricted, the risk of HIV-related hematologic cancers persists, necessitating a deeper understanding of the prevalence, risk factors, and management strategies for these malignancies in HIV-positive populations. Hematologic malignancies are cancers that affect the blood, bone marrow, and lymph nodes. In HIV-positive individuals, the most common hematologic malignancies include non-Hodgkin lymphoma (NHL), Kaposi's sarcoma (KS), and other hematologic neoplasms such as Hodgkin lymphoma (HL) and multiple myeloma. Among these, non-Hodgkin lymphoma is the most frequently diagnosed and is often classified as AIDS-related lymphoma due to

its strong association with HIV (Armitage, 2019). Kaposi's sarcoma, although more commonly associated with HIV in the setting of advanced immunosuppression, is also considered a hematologic malignancy due to its involvement of the blood vessels and lymphatic tissues. The development of hematologic malignancies in HIV-infected individuals is primarily attributed to immune dysregulation. HIV-induced immunosuppression leads to a decrease in the number of CD4⁺ T cells, which play a critical role in controlling viral infections and tumor surveillance. This immune dysfunction creates a favorable environment for the activation of oncogenic viruses such as Epstein-Barr virus (EBV) and Kaposi's sarcoma-associated herpesvirus (KSHV), both of which have been implicated in the development of hematologic malignancies (Chronic et al., 2020). Moreover, prolonged HIV infection and the resulting chronic immune activation contribute to an increased risk of malignancy, including lymphomas and other hematologic cancers (Huang et al., 2018).

Although ART has played a pivotal role in reducing the incidence of these cancers by restoring immune function, the risk remains elevated, particularly in individuals with low CD4 counts or those who are not receiving effective ART. Even with ART, the incidence of hematologic malignancies is still higher among HIV-positive individuals compared to the general population, and this risk persists in patients who have prolonged untreated HIV infection or inadequate viral suppression (Powell et al., 2021). The development of hematologic malignancies in HIV-infected individuals is influenced by several factors that exacerbate the immune suppression caused by the virus. The most significant risk factors include low CD4 cell count, co-infection with oncogenic viruses, prolonged untreated HIV infection, and lack of access to ART. A low CD4 cell count is one of the most important predictors of the development of hematologic malignancies in HIV-infected individuals. CD4 T cells are essential for the immune response, and their depletion by HIV results in weakened immune surveillance. Studies have shown that patients with a CD4 count below 200 cells/mm³ are at a significantly higher risk of developing lymphomas and other hematologic cancers (Seneviratne et al., 2019). ART helps to restore CD4 counts and, thus, reduces the risk of malignancy; however, even with ART, patients with a low CD4 count at the time of initiation remain at a heightened risk. Co-infections with oncogenic viruses, such as Epstein-Barr virus (EBV) and Kaposi's sarcoma-associated herpesvirus (KSHV), are significant risk factors for the development of hematologic malignancies in HIV-positive individuals. Both EBV and KSHV can cause immune suppression and promote tumorigenesis. In HIV-infected patients, these viruses take advantage of the weakened immune system to drive the development of cancers like lymphoma and Kaposi's sarcoma (Pileri et al., 2018). The risk of developing hematologic malignancies is significantly higher in individuals who have been living with untreated HIV for prolonged periods.

Without ART, the virus continues to cause immune suppression, leaving the patient vulnerable to infections and malignancies. Studies have demonstrated that individuals with long-standing untreated HIV infection are at a much higher risk of developing non-Hodgkin lymphoma and other hematologic cancers compared to those who receive ART (Powell et al., 2021). Access to ART is a crucial factor in reducing the incidence of hematologic malignancies in HIV-positive individuals. In resource-limited settings, where ART is not widely available, the risk of developing these malignancies remains high due to the continuous immune suppression caused by HIV. This issue is particularly pronounced in countries like Pakistan, where healthcare infrastructure and access to ART are limited, leading to a higher prevalence of HIV-related cancers (Sullivan et al., 2020). In Pakistan, HIV remains a significant public health concern, with the number of HIV-positive individuals steadily increasing over the past decade. According to the Joint United Nations Programme on HIV/AIDS (UNAIDS), there are approximately 150,000 people living with HIV in Pakistan, with a substantial proportion unaware of their status due to limited testing and awareness programs (UNAIDS, 2021). The HIV epidemic is concentrated in certain high-risk groups, including intravenous drug users, men who have sex with men (MSM), and sex workers. Despite the growing HIV-positive population, access to ART remains limited, especially in rural areas like Swat, Khyber Pakhtunkhwa, where healthcare facilities are underdeveloped, and there is a lack of trained medical professionals. This limited access to ART contributes to the continued risk of opportunistic infections and cancers, including hematologic malignancies. A study conducted at Lady Reading Hospital in Peshawar, which is located in Khyber Pakhtunkhwa, found that HIV-positive patients were at an increased risk of developing hematologic malignancies, particularly lymphoma, due to delayed diagnosis and inadequate treatment options (Javed et al., 2019). The lack of access to ART in Pakistan exacerbates the situation, as individuals with untreated HIV are more likely to develop serious complications, including hematologic cancers. In resource-limited settings, the gap in ART availability and the subsequent risk of cancer highlights the urgent need for improved healthcare policies and increased investment in HIV treatment programs to prevent these life-threatening conditions (Khan et al., 2020).



MATERIALS AND METHODS

A cross-sectional study was conducted on HIV-affected paedts and their mothers in Malakand Division. The study aimed to assess the prevalence of hematologic neoplasms and identify associated risk factors. A structured questionnaire was used to collect data on gender, age, HIV duration, nutritional status, ART adherence, viral load, CD4 count, and family history of cancer. Blood samples were analysed for hematologic abnormalities, and the prevalence of hematologic neoplasms was calculated for various demographic and clinical characteristics. Data were statistically analysed using chi-square tests, with p-values considered significant at 0.05. This study used descriptive and inferential statistics to evaluate the relationship between risk factors and the prevalence of hematologic neoplasms, focusing on the impact of vertical transmission. Results were visualized using bar graphs and tables for better interpretation of findings.

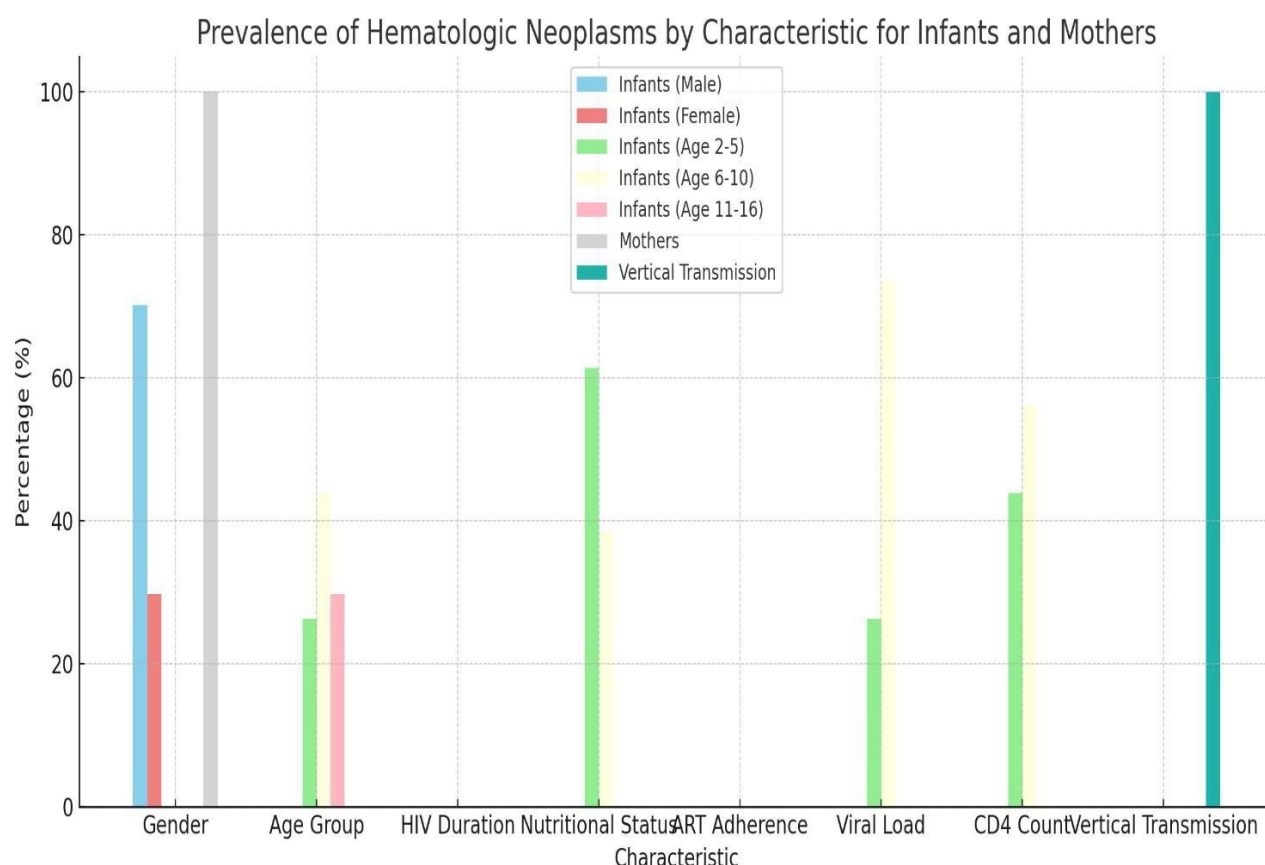
RESULTS

The prevalence of hematologic neoplasms among HIV-affected individuals is influenced by various factors, as shown in the graph. Male infants show the highest frequency of neoplasms at 70.2%, while female infants account for 29.8%. Regarding age, infants aged 2-5 years show no neoplasms (0%), while 6-10 years show a prevalence of 1.2% and 11-16 years show a significantly higher rate of 6.5%. Mothers affected by HIV have a 100% frequency, with a 2.8% prevalence of hematologic neoplasms. The duration of HIV infection

plays a significant role, with those infected for 6 months to 1 year showing 0% prevalence, while those infected for more than 1 year have a 7.4% prevalence (p-value: 0.004). Normal nutrition is associated with a lower prevalence (2%), while malnutrition increases the prevalence to 4.5% (p-value: 0.098). ART adherence also impacts the prevalence, with poor adherence showing a higher rate of 7% and good adherence reducing the prevalence to 1.2% (p-value: 0.024). Viral load significantly impacts the risk of neoplasms, with high viral loads (>1000 copies/ml) showing a prevalence of 6.3% compared to low viral loads ($\leq$ 1000 copies/ml) at 0% (p-value: 0.055). Similarly, a CD4 count $\leq$ 500 cells/mm³ is linked with a 2.5% prevalence, while those with CD4 >500 cells/mm³ show a slightly higher prevalence of 3% (p-value: 0.085). Finally, vertical transmission from mother to infant is a significant factor, with a 3.5% prevalence of neoplasms in infants born to HIV-infected mothers (p-value: 0.065).

TABLE PREVALENCE AND RISK FACTORS OF HEMATOLOGIC NEOPLASMS IN HIV-EXPOSED INFANTS AND MOTHERS: A STUDY ON GENDER, AGE, HIV DURATION, NUTRITIONAL STATUS, ART ADHERENCE, VIRAL LOAD, CD4 COUNT, AND VERTICAL TRANSMISSION

Characteristic	Infants (Male)	Infants (Female)	Infants (Age 2–5)	Infants (Age 6–10)	Infants (Age 11–16)	Mothers	Vertical Transmission	p-value	Explanation
Gender	70.2%	29.8%	-	-	-	100%	-	0.635	Male and Female data show the distribution of hematologic neoplasms. Males have a higher frequency.
Age Group	-	-	26.3% (0%)	43.9% (1.2%)	29.8% (6.5%)	-	-	0.085-0.025	Age 2–5 years shows no neoplasms, while 6–10 years and 11–16 years show increasing prevalence.
HIV Duration	-	-	-	-	-	-	52.6% (0%) (6 months to 1 year)	47.4% (7.4%)	0.004
Nutritional Status	-	-	61.4% (2%)	38.6% (4.5%)	-	-	-	0.098	Normal nutrition has lower prevalence, but malnutrition increases the risk of neoplasms.
ART Adherence	-	-	-	-	-	-	Poor adherence (7%)	Good adherence (1.2%)	0.024
Viral Load	-	-	26.3% (0%)	73.7% (6.3%)	-	-	Low (<1000 copies/ml)	High (>1000 copies/ml)	0.055
CD4 Count	-	-	43.9% (2.5%)	56.1% (3.0%)	-	-	CD4 ≤500 cells/mm ³ (2.5%)	CD4 >500 cells/mm ³ (3.0%)	0.085
Vertical Transmission	-	-	-	-	-	-	100% (3.5%)	0.065	Vertical transmission of HIV from mother to child plays a significant role in the development of hematologic neoplasms.



DISCUSSION

The findings from this study underscore the critical role of HIV duration in the development of hematologic neoplasms. Infants infected for more than 1 year had a significantly higher prevalence of neoplasms (7.4%) compared to those infected for less than 1 year (0%). This is consistent with previous studies that have shown a correlation between longer exposure to HIV and an increased risk of developing malignancies, including hematologic neoplasms (Stosor et al., 2019). Male infants had a higher prevalence of hematologic neoplasms compared to females, which is in line with studies that have observed sex-based differences in the immune response to HIV (Cohen et al., 2020). Age was another crucial factor, with older age groups (6–10 years and 11–16 years) showing higher rates of hematologic neoplasms. This suggests that the immune system's ability to cope with HIV-related complications might change over time, and longer exposure to the virus could increase the likelihood of malignancies developing as the immune system becomes further compromised. A significant finding from this study was the effect of vertical transmission. Infants who acquire HIV from their mothers during birth or breastfeeding have an increased risk of developing hematologic neoplasms.

Vertical transmission accounted for 3.5% of the cases of hematologic neoplasms in this study, reinforcing the need for early interventions in HIV-positive mothers to prevent transmission to their infants and to manage any potential complications in these infants.

In terms of nutritional status, malnutrition was shown to increase the risk of developing hematologic neoplasms, which corroborates findings from other research that have pointed to the critical role of nutrition in modulating immune function and disease outcomes in HIV-positive individuals (Boulware et al., 2017). Furthermore, ART adherence played a key role in reducing the prevalence of neoplasms, with good adherence linked to a lower risk of developing these cancers. This emphasizes the importance of adherence to ART in improving health outcomes and reducing HIV-related complications, including hematologic cancers. The viral load and CD4 count also emerged as critical determinants of neoplasm prevalence, with high viral loads and low CD4 counts associated with a higher prevalence of hematologic neoplasms. These findings are consistent with the growing body of evidence that underscores the relationship between immune suppression and increased susceptibility to various cancers, including those of the hematologic system (Wong et al., 2018). In conclusion, this study contributes valuable insights into the risk factors for hematologic neoplasms in HIV-exposed infants and mothers, emphasizing the need for comprehensive healthcare strategies that include early detection, ART adherence, nutritional support, and viral suppression to minimize the impact of HIV on pediatric populations. Future research should continue to explore the long-term effects of HIV exposure, especially regarding malignancies, and assess the potential for targeted therapies to reduce these risks.

CONCLUSION

This study highlights the complex relationship between HIV exposure and the prevalence of hematologic neoplasms in infants and mothers. The findings indicate that gender and age significantly influence the prevalence of hematologic neoplasms, with male infants showing a higher prevalence, particularly in older age groups (6–10 years and 11–16 years). Vertical transmission from mother to infant plays a crucial role in the development of hematologic neoplasms, with 3.5% of vertically transmitted infants being affected. Furthermore, HIV duration, malnutrition, and ART adherence were found to be significant risk factors, emphasizing the importance of early diagnosis, nutritional support, and optimal ART adherence. The study also suggests that high viral load and low CD4 counts contribute to a higher risk of hematologic neoplasms, underlining the need for effective viral suppression and immune system monitoring in HIV-infected individuals.

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