Human T-Lymphocyte Virus and the Development of Adult T-Cell Leukemia/Lymphoma

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Abstract

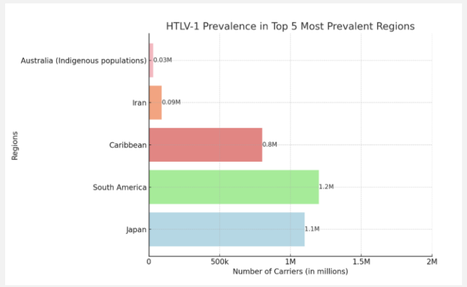
Human T-Lymphocyte Virus type I (HTLV-I) is an oncogenic virus that has been associated with the development of Adult T-cell Leukemia/Lymphoma (ATL). It has been found that HTLV causes ATL through a complex multi-step process that includes factors such as viral persistence, genetic mutations, epigenetic changes and the involvement of viral proteins that include Tax and HTLV-1 bZIP factor (HBZ). In our research, we further analyze the relationship between HTLV-1 infection in childhood and the development of ATL by looking at factors that play an important role such as prevalence, the tropic development process of ATL as well as the epigenetic changes of HTLV-1.

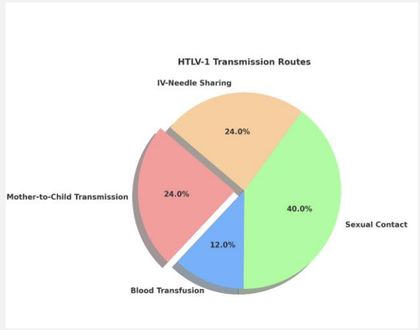
Introduction

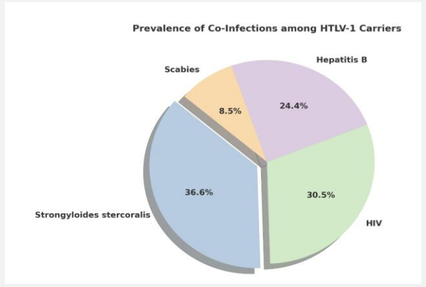
HTLV-1 is a retrovirus that causes ATLL. Even amongst those infected in childhood, early onset of HTLV-1 related diseases is rare. The virus can be transmitted via the body fluids of an infected individual through breastfeeding, vertical transmission, sexual contact, intravenous drug use and blood transfusions. Vertical transmission is more commonly associated with the development of Adult T -cell leukemia/lymphoma. (ATLL). HTLV-1, after initial transmission, can remain dormant in the host genome for several decades as a provirus, an inactive viral form integrated into the genes of the hosts cell which it can easily do using its own machinery as a retrovirus, giving the host a persistent and lifelong infection.

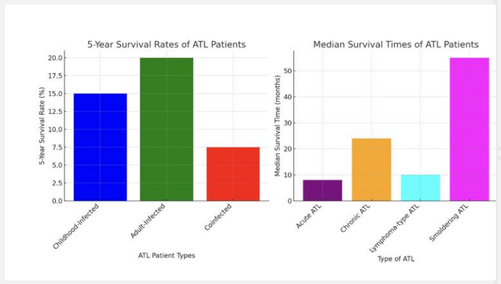
Methods

A narrative review was conducted to analyze the incidence of HTLV-1 in children and the development of ATLL. A literature review search was conducted using Saint James School of Medicine's library resources, JAMA Network Open, etc. The text word words "Human T-Lymphotropic Virus", "childhood", "T-cell Leukemia/Lymphoma", "adult" etc. The inclusion criteria consisted of scholarly or peer-reviewed source, relevant articles within the last 50 years, articles published in the English language only etc. There were 423 articles identified that consisted of quantitative and qualitative studies, 385 were excluded by abstract The remaining 38 articles were retrieved and discussed to evaluate if the literature focused on the topic area. Of the 38 articles chosen, 38 were selected because they contained relevant literature pertinent to the narrative review.









Results

This narrative review was an important look at the development of ATLL in children infected with HTLV-1. Interpreting the results was vital to emphasize the consequence of the findings. 4 figures were used to illustrate identified areas of importance that were correlated with HTLV-1 and ATLL. Table 1 through Table 4 illustrate data that was identified are relevant and analyzed to determine if significant changes for at-risk children being exposed to HTLV-1 would make a difference societally. The results of this narrative review revealed that children in HTLV-1 endemic societies had a greater risk of experiencing infections and its sequelae depending on when infected, viral load and means when exposed to repetitive sources of the HTLV-1 virus reservoirs in endemic areas.

Discussion

ATLL is malignancy of regulatory T cells caused by HTLV-1. In Chang et al primary ATLL cells, viral proteins appear just after an infection. Integration sites of the provirus into host genome are random with complex genetic abnormalities. Tax and HBZ are vital for ATLL progression. Tax is present in early and late stages of HTLV-1 infection. Tax's ensuing inhibition of DNA repair mechanisms, and downregulation of MHC class I molecules, all help the virus evade the immune system was noted in Nakahataet et al. This evasion helps HTLV-1 infected cells avoid immune detection and elimination. Durer and Babiker noted that HBZ augments the long-term survival and proliferation of HTLV-1 using the CREB pathway, promoting antiapoptotic genes and downregulates genes: CXCL10 and CIITA this further helps avoid immune detection. Angham and Ratner saw all these actions by HTLV-1 proteins are critical for the survival and proliferation of infected cells. In Marçais et al HBZ is expressed in all ATLL cases, whereas Tax expression is heterogeneous. Bangham emphasized that HBZ is the viral gene responsible for leukemogenesis leading to genetic and epigenetic changes in host genes. According to Giam and Semmes, host immune responses to Tax are implicated in the heterogeneity of pathogenesis in lymphomatous neoplasm.

Conclusion

HTL1 plays a critical role in the development of ATL. Central to this process is the Tax protein that influences the pathogenesis of ALT. Findings show that ATL is a single disease linked to HTL—1 and shares diverse molecular abnormalities. Clonal selection happens during ATL progression due to clonal evolution. Recent studies have identified genomic features of proviral integration sites and proviral structures that influence expansion of Tax protein in ATL cells. ATLs exhibit significant genomic stability. Primary cause for instability is due to HTLV-1 viral oncoprotein, Tax. Tax activates viral transcriptase but also impairs dsDNA break repair. Some develop ATL because HTLV-1 infection drives both cell proliferation and leukemia development. Virus promotes cell proliferation to enhance survival, facilitated by inefficient transmission through infected cells.

Resources

Giam, C.-Z.,; Semmes, O. J. (2016). HTLV-1 infection and adult T- cell leukemia/lymphoma—A tale of two proteins: Tax and HBZ. Viruses, 8(6), 161. https://doi.org/10.3390/v806016