ARTICLE
JOURNAL OF UNIVERSITY OF BABYLON
For Pure and Applied Sciences (JUBPAS)
Vol.3; No.32.| 2024

Role of HTLV-1 Infection in Hematologic Cancer Patients In Hillah City, Iraq; Studying the Function of the *tax/rex* Gene in HTLV-1-Associated Chronic Myeloid Leukemia

Samara Kadhim Hadi[1], Ali H. Al-Marzoqi[2*] and Zainab W Al-Maaroof[3]

[1] Babylon University, College of Science for Women, Biology Department. samara.almaamory.gsci154@student.uobabylon.edu.iq. Al-Hillah, Babil, Iraq.

[2] Babylon University, College of Science for Women, Biology Department. almarzoqiali@uobabylon.edu.iq. Al-Hillah, Babil, Iraq

[3] Babylon University, College of Medicine, Pathology Department. zainab_19771961@uobabylon.edu.iq. Al-Hillah, Babil, Iraq.

***Corresponding author email:** almarzoqiali@uobabylon.edu.iq; mobile: 07702818558

دور عدوى الفيروس اللمفاوي التائي البشري HTLV-1 في مرضى سرطان الدم في مدينة الحلة، العراق؛ دراسة وظيفة الجين *tax/rex* في سرطان الدم النخاعي المزمن المرتبط بـ HTLV-1

سمارة كاظم هادي[1]، علي حسين المرزوكي[2*] وزينب وهاب المعروف[3]

[1]جامعة بابل، كلية العلوم للبنات، قسم علوم الحياة. samara.almaamory.gsci154@student.uobabylon.edu.iq. الحلة. بابل. العراق

[2]جامعة بابل، كلية العلوم للبنات، قسم علوم الحياة. almarzoqiali@uobabylon.edu.iq. الحلة. بابل. العراق

[3]جامعة بابل، كلية الطب، قسم علم الأمراض. zainab_19771961@uobabylon.edu.iq. الحلة. بابل. العراق

Accepted: 9/7/2024 **Published:** 30/9/2024

ABSTRACT

Background: About 5-10 million people worldwide have HTLV-1, which causes ATLL, HAM/TSP, and inflammation. HTLV-1, first human retrovirus. HTLV-1's role in hematologic and non-hematologic cancers is uncertain.This study studied the prevalence of HTLV-1 infection in hematologic and non-hematologic malignancies and the role of Pol and tax/rex genes in cancer.

Materials and Methods: The study included 83 leukemia patients and 25 healthy people. Serological and molecular testing was done on 49 males and 59 women aged 20–80. Blood and serum from controls and patients were tested. Lab, clinical, and genetic tests indicated healthy Babylonian Iraqi 20–80-year-olds. Human genomic RNA was isolated from patient and control whole blood cultures. The US-developed Promega human genomic RNA extraction kit collected RNA and DNA from research participants and healthy controls' entire blood samples. GoTaq® 1-Step RT-qPCR enhances genes.

Results: Shows leukemia types and cases. ALL had 8, 9, 4, and 7, CML 64 (77.1%). Statistics on gender leukemia. Men outnumbered women in CML 37/83 (44.6%) to 27/83 (32.5%). Cancer is mostly male except ALL (4.8%) and CML (44.6%). Age and leukemia subtypes. Leukemia patients (82.1%) and controls (0.9%) had higher HTLV-1/Pol and Tax-Rex genotype frequencies than healthy people (P = 0.1, OR 2.1). Genes Pol and Tax-Rex induced CML. The study found 58.5% of CML patients received Pol and 23.6% Tax-Rex.

Conclusions: Tax/rex genes are supposed to suggest cancer connected with pol genes, hence there is a substantial correlation between this gene and chronic myeloid leukemia (CML) compared to healthy people.

Keywords: HTLV-1; malignancy; *Pol*; *tax*/*rex*; malignancies; Hillah city and CML.

ISSN: 2312-8135 | Print ISSN: 1992-0652
info@journalofbabylon.com | jub@itnet.uobabylon.edu.iq | www.journalofbabylon.com

ISSN: 2312-8135 | Print ISSN: 1992-0652
info@journalofbabylon.com | jub@itnet.uobabylon.edu.iq | www.journalofbabylon.com

INTRODUCTION

Tax is the primary protein involved in the cancerogenesis of host cells, and HTLV-1 has been linked to various cancers. But scientists still not know enough about the exact genes that Tax impact in cancer and how those genes interact with one another to speed up the disease's development. Therefore, the goals of this research are to [1] identify the unique characteristics of HTLV-1 and [2] understand its overall impact on various malignancies by clarifying the protein-protein interactions that occur during an HTLV-1 infection. A kind of leukemia and lymphoma that affect adult T cells, the human T-lymphotropic virus (HTLV) is a retrovirus [1]. It has been found that there are four different kinds of HTLV: HTLV-1, HTLV-2, HTLV-3, and HTLV-4. The viral proteins that are encoded in the HTLV-1 genome contribute to the infection's ability for cells to multiply and survive [2]. Three genes that help with replication are encoded by this genome: Gag, Pol, and Env. The splicing of viral messenger RNA is regulated by Rex. Several pathways, including CREB/ATF, NF-źB, AP-1, and SRF, regulate the expression of viral and cellular genes via Tax. It is thought to be pivotal in the ATL process and regulates various cellular activities, such as protein binding, transcriptional activation and repression, and dysregulation of the cell cycle and genomic integrity maintenance, which in turn promote cell proliferation and resistance to apoptosis. HTLV's Incidence in Various Malignancies It has been discovered that HTLV-1 is associated with several cancers, such as pancreatic cancer, chronic myeloid leukemia, biliary tract cancer, esophageal cancer, stomach cancer, colorectal cancer, liver cancer, lung cancer, glioblastoma, and the list goes on [3] [4]. Although HTLV-1 proviral RNA has been detected in cancer cells and linked to inflammation in these organs, little is understood about the pathways that cause inflammation and cancer, including how viral and cellular proteins interact [5] . In 1979, scientists found the first human retrovirus, human T-lymphotropic virus type 1 (HTLV-1) [6]. The first documented case of HTLV-1 infection in a cutaneous T-cell lymphoma patient. Breastfeeding, sexual contact, and blood contact are the three main routes of transmission for this retrovirus [7].

A connection between HTLV-1 infection and adult T-cell leukemia/lymphoma (ATL), HTLV-1 associated myelopathy / tropical spastic paraparesis (HAM/TSP), and HTLV-associated uveitis (HAU) has been shown in epidemiological evidence. Although many carriers have no symptoms

ISSN: 2312-8135 | Print ISSN: 1992-0652
info@journalofbabylon.com | jub@itnet.uobabylon.edu.iq | www.journalofbabylon.com

throughout their lives, HTLV-1 can induce opportunistic co-infections including TB and strongyloidiasis because of its immunosuppressive effect. Although the precise number of seropositive individuals globally cannot be determined due to a lack of data, the global prevalence of HTLV-1 is estimated to be around 15-20 million people.6 Several countries in sub-Saharan Africa, parts of Iran, and Melanesia are endemic, as are parts of southwestern Japan and the Caribbean basin [8]. Mashhad was added to the list of HTLV-1 endemic regions in Iran in 1996.8,9 Research in Iran has shown that the prevalence rates of HTLV-1 infection vary by location and by population subset (e.g., blood donors, thalassemia major patients, etc.) [9]. There is limited evidence regarding the frequency of HTLV-1 infection in other cancers in Iran, such as stomach, colon, breast, and lung cancers, although there is some evidence linking HTLV-1 infection to hematologic malignancies like ATL and lymphosarcoma T-cell leukemia [10] [11]. There are an estimated 5–10 million people infected with the human T-cell lymphotropic virus type 1 (HTLV-1) worldwide [12]. Many of these people may be asymptomatic carriers who inadvertently transmit the virus from generation to generation. Many instances go unreported in densely populated areas like China, India, Northwest Africa (i.e., the Arab Maghreb), and East Africa, hence it's probable that the real figure is higher due to poor universal screening. The true global frequency might be as high as 20 million, according to estimates. Some countries, like Japan, Australia, Iran, Jamaica, and Colombia, have pockets of extremely endemic areas where the virus can spread locally. Up to 5% of infected individuals have adult T-cell leukemia/lymphoma (ATLL) and 3.8% have HTLV-1-associated myelopathy/tropical spastic paraparesis (HAM/TSP) [13].

MATERIALS AND METHODS

From September 2023 to April 2024, researchers from Merjan Teaching Hospital's hematology and medical oncology ward carried out this cross-sectional study. This study encompassed all patients who had a confirmed diagnosis of a hematologic condition, including cancer (CML, ALL, AML, and CLL) and myelofibrosis. Cancers of the colon, breast, ovary, stomach, lung, etc., were also invited to participate in the study; however, these instances were excluded. After receiving both written and verbal information, patients were able to make an informed decision. The 1975 Declaration of Helsinki established ethical standards that were followed by the research protocol. Each participant in this trial had approximately 5 mL of venous blood drawn. Separate tubes containing EDTA were used to collect one portion of the blood (about two milliliters). To prepare

the second portion of the blood for the immunological assay, it was centrifuged at 3000 rpm for 15 minutes after being placed in a gel tube for 30 minutes. The serum was then collected and stored in the freezer at -20 ºC. To determine whether the participants had the HTLV-1 specific gene, a qrt PCR (Promega, USA) was used. At the Iraqi Blood Transfusion Organization, we frequently screen for HTLV-1 infection in our lab. The University of Babylon/College of Science for Women ethics committee gave their blessing to this research.

Patients and Healthy control group

The study included 83 patients with leukemia and 25 healthy individuals who did not have the disease. Researchers used serological and molecular testing to identify 19 men and 44 females, with ages ranging from 20 to 80, who were subsequently included in the study. The controls and all patients' blood and serum samples were examined with great care. Participants ranged in age from 20 to 80 and were all deemed healthy according to laboratory, clinical, and genetic criteria; they were recruited from the Babylonian Iraqi community.

Blood samples collection & Control Samples collection

Each participant in this trial had approximately 5 mL of venous blood drawn. Separate tubes containing EDTA were used to collect one portion of the blood (about two milliliters). To prepare the second portion of the blood for the molecular assay, it was centrifuged at 3000 rpm for 15 minutes after being placed in a gel tube for 30 minutes. The serum was then collected and stored in the freezer at -20 ºC.

Collecting control samples

Fifty healthy adults, both male and female, with an age distribution comparable to the patients were venipuncture for blood samples.

RNA extraction

For molecular studies, genomic RNA is extracted from blood in EDTA tubes; for samples taken from frozen blood, we using proteinase K applied with Geneaid kit. In the Estimation of RNA Concentration and Purity (Quantitative), Using the Protocol for RNA Separation from Whole Blood Samples of Patients and Control Subjects, human genomic RNA was isolated from both patient and control whole blood cultures. A human genomic RNA extraction kit developed by Promega in the USA was used to isolate RNA and DNA from whole blood samples taken from

ISSN: 2312-8135 | Print ISSN: 1992-0652 | www.journalofbabylon.com | jub@itnet.uobabylon.edu.iq | info@journalofbabylon.com

both study participants and healthy controls. To estimate the RNA concentration in the samples, 2.5µl of the extracted RNA was put into the Nano drop, which measures concentration in ng/µL. To detect protein contamination, the ratio of optical density (OD) 260/280 nm was noted (Thermo Fisher Scientific). In order to purify RNA, the recommended 260/280 ratio ranged from 1.7 to 1.9 [14].

RNA Electrophoresis (Qualitative RNA Estimation) and rt-qPCR:

After genomic RNA extraction, HTLV 1/ pol F; CAGCCCCTTCACAGTCTCTACTG, R; AGAAGGATTTAAATATATTTGGTCTCGG and HTLV 1 tax1/rex1; F; ATCCCGTGGAGACTCCTCAA, R; AACACGTAGACTGGGTATCC were used to confirm the proximity and orientation of the separated RNA (Sambrook and Maniatis, 1989). GoTaq® 1-Step RT-qPCR System used for converting and amplification the targeted genes. Blending Expert twenty microliters of RNase-free water, four microliters of Oligo dT, and one microliter of random or particular primer. Once the mixture has been delicately mixed with a pipette, it can be processed into the PCR machine and operated in accordance with the following program: 37˚C for 15~30 minutes, followed by 85C for 5 minutes.

STATISTICAL ANALYSIS

The data was examined with the help of IBM's SPSS program, version 29, located in New York, USA. Normally distributed data are shown as mean ± SD, while no normally distributed data are shown as median (range) [15]. The frequency of HTLV-1 infection was compared between patients with hematologic diseases and those with non-hematologic malignancies using a chi-square test or Fisher's exact test.

ETHICAL APPROVAL

Ethical standards derived from the Declaration of Helsinki were followed throughout the research. Prior to sample collection, the procedure was carried out with the patients' verbal and analytical consent. A local ethics committee examined and approved the study protocol, subject information, and permission form in accordance with document number 20, which includes the number and the date in 20-7/5/2024.

ISSN: 2312-8135 | Print ISSN: 1992-0652 | info@journalofbabylon.com | jub@itnet.uobabylon.edu.iq | www.journalofbabylon.com

ISSN: 2312-8135 | Print ISSN: 1992-0652
info@journalofbabylon.com | jub@itnet.uobabylon.edu.iq | www.journalofbabylon.com

RESULTS AND DISCUSSION

Figure 1 displayed the different types of leukemia and the total number of cases that were gathered for this study. Among these types, CML had the highest proportion at 64 (77.1%), followed by CLL at 8 (9.6%), AML at 4 (4.8%), and ALL at 7 (8.4%).

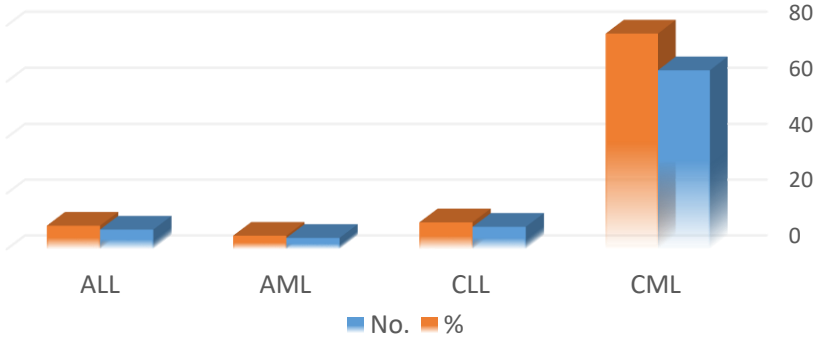

Figure 1: type of leukemia investigated in this study

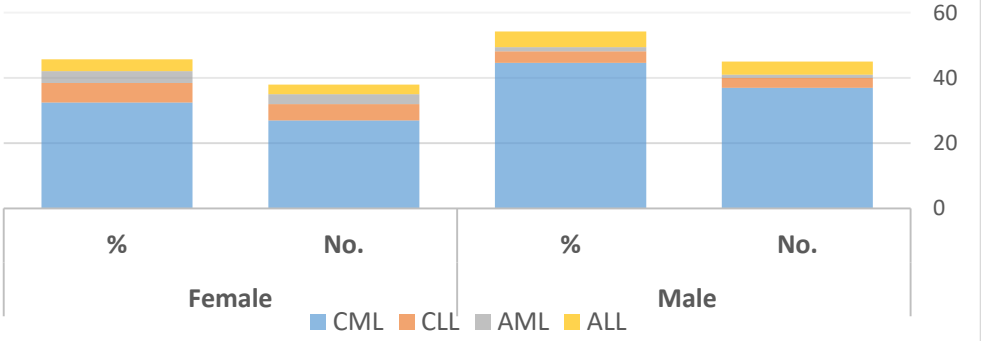

Figure 2: distribution the types of leukemia according to sex

Figure 2 and 3 shows the distribution of leukemia cases by sex and age. It is worth noting that the highest ratio among CML was 37/83 in males (44.6%) and 27/83 in females (32.5%), indicating that there were more males than females. Males make up a disproportionately large percentage of the cancer population across all subtypes, but especially in CML (44.6%) and ALL (4.8%). According to research conducted in Western countries, males make up the majority across all categories and subcategories [16].

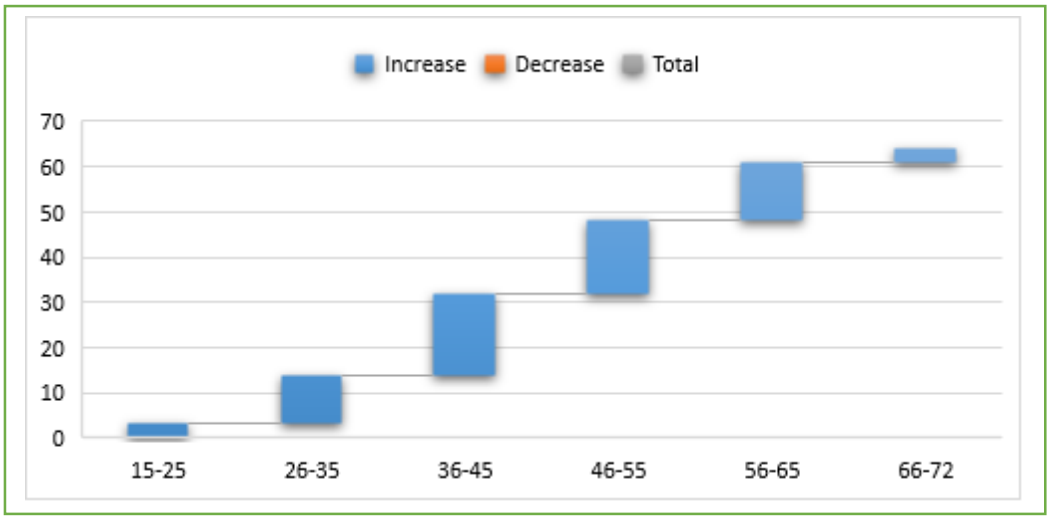

Figure 3: Type of leukemia associated with Age group

Whether this is the case for males and females depends on their exposure to the environment. According to previous study, there is a noticeable surge in the age distribution of ALL in developed countries between 1-12 years old. A third of all cases of leukemia in Kenya and Yamen were in children younger than fifteen years old [17] [18]. The age distribution of CML in Al Hillah city also peaks between 1-10 years, followed by 11-20 years, according to our study.

ISSN: 2312-8135 | Print ISSN: 1992-0652
info@journalofbabylon.com | jub@itnet.uobabylon.edu.iq | www.journalofbabylon.com

ISSN: 2312-8135 | Print ISSN: 1992-0652
info@journalofbabylon.com | jub@itnet.uobabylon.edu.iq | www.journalofbabylon.com

In 2023, there were more cases of chronic myeloid leukemia (CML) than in previous years, and the study also found a higher percentage of leukemia cases in Babil province than in other cancer centers, which may be attributable to the region's larger population. Most instances were found between the ages of 36 and 56 (13 each), as shown in figure 3, which reveals the types of leukemia related with age groups. The genotype frequency of the HTLV-1/Pol and HTLV-1/Tax-Rex genes was found to be significantly higher in the leukemia group compared to the healthy group (82.1% for the patients, P = 0.01, OR 0.3; 0.9% for the controls, P = 0.1, OR 2.1). CML was found to be the major percentage genotype in both the /Tax-Rex and Pol genes.

Among all instances in the study, CML patients made up the majority with Pol (58.5%), while Tax-Rex accounted for 23.6% as revealed in table 1. While chronic myelogenous leukemia (CML) develops slowly over time, acute myeloid leukemia (AML) spreads rapidly and is incurable. Three distinct phases of virus can be seen as stages of the disease: chronic, rapid, and blast. A patient's leukemia progresses slowly but surely when it is chronic. Immature blood cells are a hallmark of stage two, the extended stage. Stage three, "the explosion," is the last one.

A kind of myeloproliferative tumor, chronic myeloid leukemia (CML) is characterized by the dysregulated production and uncontrolled proliferation of mature and maturing granulocytes, which ordinarily differentiate properly. The majority of cases encompass the BCR-ABL1 fusion gene, which arises from the reciprocal movement of chromosomes 9 and 22 (t9;22) (q34; q11).

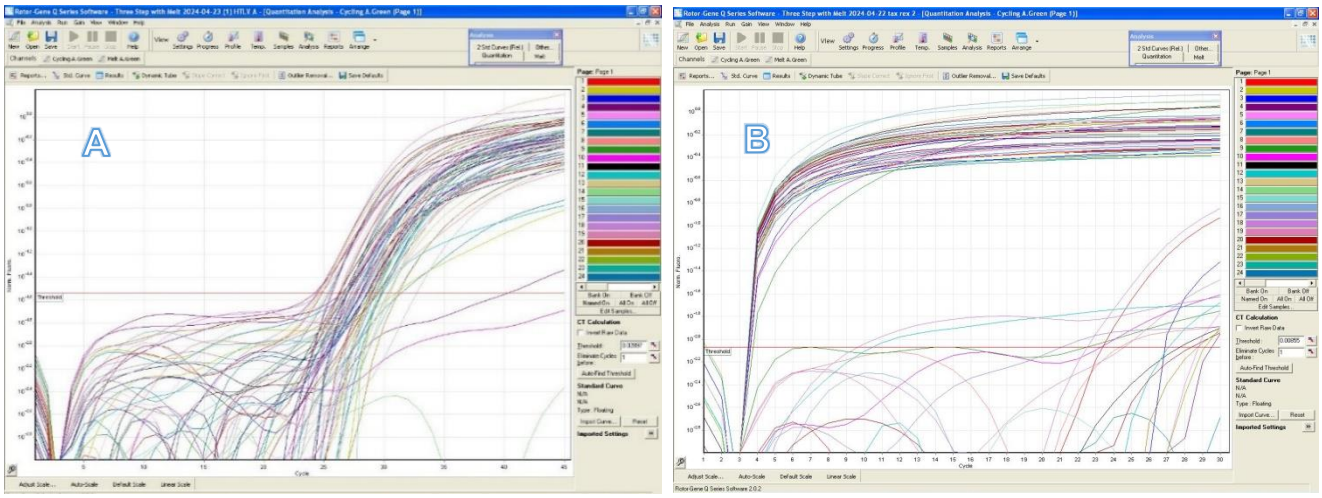

Figure 4: rt-qPCR results using Rotergen (Qiagen), A; results of Pol HTLV-1, while B; revealed results of *Tax/Rex* gene results

ISSN: 2312-8135 | Print ISSN: 1992-0652
info@journalofbabylon.com | jub@itnet.uobabylon.edu.iq | www.journalofbabylon.com

We present here an extremely unusual case of chronic myeloid leukemia with variable cytogenetics [19].

About 50% of people with chronic myeloid leukemia who have no symptoms can be diagnosed with a complete blood count alone. Right now, the chronic phase is impacting the vast majority of CML patients. Splenomegaly and anemia are hallmarks of chronic myeloid leukemia's chronic phase.

Symptomatic anemia manifests as a lack of energy and a generally listless state. Signs of a mass effect due to splenomegaly include early fullness, discomfort, or fullness in the left upper quadrant. In addition, CML can cause platelet dysfunction or thrombocytopenia, which can lead to bleeding. It can also cause basophilia to release histamine, thrombosis or priapism, and ulcers in the upper gastrointestinal tract. When chronic myeloid leukemia is in its rapid or blast phase, symptoms such as lymphadenopathy, fever, joint pain, bleeding, infections, and headaches that are more likely [20].

It is not completely known how an infection with HTLV-1 leads to the development of ATLL. Because of the lengthy time it takes for an infection to cause disease progression, HTLV-1 is a great model to research multistep oncogenesis. Once an infection has occurred, viral proteins like Tax help the virus replicate and spread. In order to successfully replicate its genome, which necessitates entering and finishing the S phase of the cell cycle, HTLV-1 alters normal cellular processes [21].

Table (1): Type of leukemia associated with HTLV-1 Genes

Cases	HTLV-1 Pol Gene		HTLV-1 Tax-Rex Gene		Total	
	No.	%	No.	%	No.	%
CML	**62**	**58.5**	**25**	**23.6**	**87**	**82.1**
CLL	6	5.7	4	3.8	10	9.4
AML	2	1.9	1	0.9	3	2.8
ALL	5	4.7	0	0.0	5	4.7
Healthy	**1**	**0.9**	**0**	**0.0**	**1**	**0.9**
Total	76	71.7	30	28.3	106	100.0

virus can replicate and spread to other host cells in a few days because Tax inactivates tumor suppressors, interacts with proteins in cells to deregulate gene expression and cell cycle regulation, and inhibits DDR and apoptosis. This is all in an attempt to disable cell cycle checkpoints and promote cell cycle progression, regardless of the long-term consequences to the host cells. Therefore, the virus is unaffected by the accumulation of genetic damages. The successful replication and dissemination of the virus may have resulted in these insults as an unexpected side effect. The formation of ATLL is facilitated by Tax's ability to raise the overall rate of cellular mutation. Due to the interdependence of cellular operations, there are still knowledge gaps about the ways in which Tax affects these processes, despite the extensive research on Tax's impacts on cellular processes. Improving our capacity to understand the intricate effects of Tax on cellular function networks and the fundamental stages involved in HTLV-1 driven leukemogenesis will be aided by advances in experimental methods and animal model systems [22].

ATL is a cancer that develops in adult T cells and is caused by viruses. The prognosis for ATL is quite bad. We still do not fully grasp the close connection between HTLV-1 and the immunological response it induces in the front, which makes therapeutic therapy of ATL challenging [23] [24]. The host immune system and HTLV-1 proteins, including as Tax and HBZ, interact in complex ways, which lead to complicated disease pathways after HTLV-1 infection (Moles, et al., 2022). Despite a wealth of information regarding the several roles played by these viral oncoproteins, Tax and HBZ are unable to promote the growth of cancerous ATL cells in the absence of IL-10. By increasing the production of certain cytokines, both Tax and HBZ stimulate the growth of cells infected with HTLV-1 [25].

The anti-inflammatory and immunosuppressive effects of cytokines, in conjunction with this action, might be crucial in shifting HTLV-1-induced inflammation towards ATL. Impact of Tax-specific CTLs on immunological surveillance of HTLV-1 infected and ATL cells is underscored by the success of a therapeutic vaccination targeting Tax and the incredibly low levels of protein expression in ATL patients. In addition, both in vitro and in vivo studies demonstrated that targeted therapies that result in Tax breakdown were highly effective against ATL cells.

It is crucial to target both the innate immune milieu and the viral oncoproteins, according to murine preclinical models of ATL. Future research should incorporate treatments that target the HTLV-1 virus, the primary cause of ATL, and fill in the fascinating picture of host immunity/HTLV-1

ISSN: 2312-8135 | Print ISSN: 1992-0652
info@journalofbabylon.com | jub@itnet.uobabylon.edu.iq | www.journalofbabylon.com

ISSN: 2312-8135 | Print ISSN: 1992-0652 | info@journalofbabylon.com | jub@itnet.uobabylon.edu.iq | www.journalofbabylon.com

infection. The viral proteins, the cells they infect downstream, and the host immunological microenvironment, which may include non-malignant cells infected with HTLV-1, are all potential targets of these treatment strategies [24] [26].

ACKNOWLEDGMENTS

Those working in the medical oncology and hematology units of the University of Babylon's College of Science for Women's Merjan Teaching Hospital deserve particular recognition.

Conflict of interests

There are non-conflicts of interest

The writers have maintained a policy of non-disclosure throughout this inquiry.

Financial support and sponsorship disclosure

No financial information is available for the writers.

Competing interests

The writers affirm that they are not involved in any conflicts of interest.

References

[1] M, Yamagishi; D, Fujikawa; T, Watanabe; K, Uchimaru. HTLV-1-mediated epigenetic pathway to adult T-cell leukemia–lymphoma. Frontiers in microbiology. 2018 Jul 24;9:1686.

[2] G, Du; W,Zhang; Z, Zhang; M, Zeng; Y, Wang. HTLV-1-associated genes as potential biomarkers for endometrial cancer. Oncology Letters. 2019 Jul 1;18(1):699-705.

[3] V, Kouznetsova; S, Chen; I, Tsigelny. HTLV-1 can be involved in acceleration of different nonhematological cancers. Journal of cancer research and therapeutics. 2019;7:1-8.

[4] S, Nakahata; D, Enriquez-Vera; MI, Jahan; K, Sugata; Y, Satou. Understanding the Immunopathology of HTLV-1-Associated Adult T-Cell Leukemia/Lymphoma: A Comprehensive Review. Biomolecules. 2023 Oct 19;13(10):1543.

[5] Y, Ma, S, Zheng; N, Wang; Y, Duan; X, Sun; J, Jin; W, Zang; M, Li; Y, Wang ; G, Zhao. Epidemiological analysis of HTLV-1 and HTLV-2 infection among different population in Central China. PloS one. 2013 Jun 24;8(6):e66795.

[6] R,Pessôa; DR, de Souza; Y, Nukui; J, Pereira; LA, Fernandes ; RN, Marcusso; AC, de Oliveira; J, Casseb; AJ, da Silva Duarte; SS , Sanabani. Small RNA Profiling in an HTLV-1-Infected Patient with Acute Adult T-Cell Leukemia-Lymphoma at Diagnosis and after Maintenance Therapy: A Case Study. International journal of molecular sciences. 2023 Jun 26;24(13):10643.

[7] FA, Proietti; AB, Carneiro-Proietti; BC, Catalan-Soares; E, Murphy. Global epidemiology of HTLV-I infection and associated diseases. Oncogene. 2005 Sep;24(39):6058-68.

[8] H, Rafatpanah; MR, Hedayati-Moghaddam; F, Fathimoghadam; HR, Bidkhori; SK, Shamsian; S, Ahmadi; L, Sohgandi; MR, Azarpazhooh; SA, Rezaee; R, Farid; A, Bazarbachi. High prevalence of HTLV-I infection in Mashhad, Northeast Iran: a population-based seroepidemiology survey. Journal of Clinical Virology. 2011 Nov 1;52(3):172-6.

[9] Z, Mortezaie; M, Bouzari; R, Roghanian. Evaluating the frequency of HTLV-I/II infection among blood donors, major thalassemic patients and individuals infected with hepatitis B and C viruses in Isfahan, Iran. Iranian journal of blood and cancer. 2012;4(2):75-80.

[10] H, Jalaeikhoo; M, Soleymani; M, Rajaeinejad; M, Keyhani. Prevalence of human T-lymphotropic virus type 1 (HTLV-1) infection in patients with hematologic disorders and non-hematologic malignancies in a tertiary referral hospital. Archives of Iranian medicine. 2017 Apr 1;20(4):0-.

[11] Y,Tagaya; RC, Gallo. The exceptional oncogenicity of HTLV-1. Frontiers in microbiology. 2017 Aug 2; 8:1425.

[12] S, Al Sharif; DO, Pinto; GA, Mensah; F, Dehbandi; P, Khatkar; Y, Kim; H, Branscome; F, Kashanchi. Extracellular vesicles in HTLV-1 communication: the story of an invisible messenger. Viruses. 2020 Dec 10; 12(12):1422.

[13] T, Naito; JI, Yasunaga; Y, Mitobe; K, H, Shirai; Sejima; H, Ushirogawa; Y, Tanaka; T, Nakamura; K, Hanada; M, Fujii; M, Matsuoka. Distinct gene expression signatures induced by viral transactivators of different HTLV-1 subgroups that confer a different risk of HAM/TSP. Retrovirology. 2018 Dec; 15:1-20.

[14] D, Russel; J, Sambrook. Molecular cloning: a laboratory manual. New. 2001.

[15] IBM Corp. Released. IBM SPSS Statistics for Windows, Version 29.0.2.0 Armonk, NY: IBM Corp. 2023.

[16] MA, Abdulla; A, Amer; Z, Nawaz; AS, Abdullah; A, Al-Sabbagh; S, Kohla; AJ, Nashwan; MA, Yassin. An uncommon case of chronic myeloid leukemia with variant cytogenetics. Acta Bio Medica: Atenei Parmensis. 2018;89(Suppl 3):28.

[17] E, Jabbour; H, Kantarjian. "Chronic myeloid leukemia: 2018 update on diagnosis, therapy and monitoring". Am J Hematol.;93(3):442-459. 2018.

[18] W, Kassahun; G, Tesfaye; LG, Bimerew; D, Fufa; W, Adissu; T. Yemane. Prevalence of Leukemia and Associated Factors among Patients with Abnormal Hematological Parameters in Jimma Medical Center, Southwest Ethiopia: A Cross-Sectional Study. Advances in Hematology. 2020;2020(1):2014152.

[19] JI, Yasunaga; M, Matsuoka. Human T-cell leukemia virus type I induces adult T-cell leukemia: from clinical aspects to molecular mechanisms. Cancer control. 2007 Apr;14(2):133-40.

[20] K, Pryor; SJ, Marriott. Pleiotropic Functions of HTLV-1 Tax Contribute to Cellular Transformation. InT-Cell Leukemia-Characteristics, Treatment and Prevention 2013 Feb 20. IntechOpen.

[21] H, El Hajj,; A Bazarbachi. Interplay between innate immunity and the viral oncoproteins Tax and HBZ in the pathogenesis and therapeutic response of HTLV-1 associated adult T cell leukemia. Frontiers in Immunology. 2022 Jul 22;13:957535.

[22] K, Tsukasaki; A, Marçais; R, Nasr; K, Kato; T, Fukuda; O, Hermine; A, Bazarbachi. Diagnostic approaches and established treatments for adult T cell leukemia lymphoma. Frontiers in Microbiology. 2020 Jun 19; 11:1207.

[23] DG, de La-Roque; EV, Santos; ES, Rodrigues; PN, da Costa; VS, Brauer; F, Almeida; TM, de Haes; OM, Takayanagui; DT, Covas; S, Kashima. The expression of tax and HBZ genes in serum-derived extracellular vesicles from HTLV-1 carriers correlates to proviral load and inflammatory markers. Frontiers in Microbiology. 2022 May 2;13:881634.

ISSN: 2312-8135 | Print ISSN: 1992-0652
info@journalofbabylon.com | jub@itnet.uobabylon.edu.iq | www.journalofbabylon.com

[24] R, Moles; S, Sarkis; V, Galli; M, Omsland; M, Artesi; M, Bissa; K, McKinnon; S, Brown; V, Hahaut; R, Washington-Parks; J Welsh. NK cells and monocytes modulate primary HTLV-1 infection. PLoS Pathogens. 2022 Apr 4;18(4):e1010416.

[25] M, Bellon; C, Nicot. Feedback loop regulation between pim kinases and tax keeps human T-cell leukemia virus type 1 viral replication in check. Journal of Virology. 2022 Feb 9;96(3):e01960-21.

[26] S, Horwitz; OA, O'connor; B, Pro; L, Trümper; S, Iyer; R, Advani; NL, Bartlett; JH, Christensen; F, Morschhauser; E, Domingo-Domenech; G, Rossi. The ECHELON-2 Trial: 5-year results of a randomized, phase III study of brentuximab vedotin with chemotherapy for CD30-positive peripheral T-cell lymphoma. Annals of Oncology. 2022 Mar 1;33(3):288-98.

ISSN: 2312-8135 | Print ISSN: 1992-0652
info@journalofbabylon.com | jub@itnet.uobabylon.edu.iq | www.journalofbabylon.com

ISSN: 2312-8135 | Print ISSN: 1992-0652
info@journalofbabylon.com | jub@itnet.uobabylon.edu.iq | www.journalofbabylon.com

الخلاصة

مقدمة: يشكل 5 الى 10 ملايين شخص في جميع أنحاء العالم يعانون من الاصابة بـ HTLV-1، الذي يسبب ATLL، HAM/TSP، والالتهاب. HTLV-1، أول فيروس قهري بشري. دور HTLV-1 في السرطانات الدموية وغير الدموية غير مؤكد. تناولت هذه الدراسة مدى انتشار HTLV-1 في الأورام الخبيثة الدموية وغير الدموية ودور جينات بول والضرائب/ريكس في السرطان.

المواد والطرق: شملت الدراسة 83 مريضاً بسرطان الدم و25 شخصاً سليماً كمجموعة سيطرة. تم إجراء الاختبارات المصلية والجزيئية على 49 رجلاً 59 امرأة وتتراوح أعمارهم بين 20 و80 عامًا. تم اختبار الدم والمصل من الضوابط والمرضى. أشارت الاختبارات المعملية والسريرية والوراثية إلى عراقيين بابليين أصحاء تتراوح أعمارهم بين 20 و80 عامًا. تم عزل الحمض النووي الريبي الجينومي البشري من المريض والسيطرة على ثقافات الدم الكاملة. قامت مجموعة Promega لاستخراج الحمض النووي الريبي الجينومي البشري التي طورتها الولايات المتحدة بجمع الحمض النووي الريبي (RNA) والحمض النووي (DNA) من المشاركين في البحث وعينات الدم الكاملة للضوابط الصحية. GoTaq® 1-Step RT-qPCR يعزز الجينات.

النتائج: يظهر أنواع وحالات سرطان الدم. كان لدى الجميع 8، 9، 4، و7، 64 CML (77.1٪). إحصائيات عن سرطان الدم بين الجنسين. فاق عدد الرجال عدد النساء في 37/83 CML (44.6٪) إلى 83/27 (32.5٪). السرطان في الغالب ذكوري باستثناء سرطان الدم النخاعي المزمن (4.8%) وسرطان الدم النخاعي المزمن (44.6%). العمر وأنواع سرطان الدم الفرعية. كان لدى مرضى سرطان الدم (82.1٪) والضوابط (0.9٪) ترددات أعلى للنمط الجيني HTLV-1 / Pol وTax-Rex مقارنة بالأشخاص الأصحاء (P = 0.1، OR 2.1). الجينات Pol وTax-Rex المستحثة بسرطان الدم النخاعي المزمن. وجدت الدراسة أن 58.5% من مرضى سرطان الدم النخاعي المزمن تلقوا علاج Pol و23.6% Tax-Rex.

الاستنتاجات: من المفترض أن تشير جينات Tax-Rex إلى وجود سرطان مرتبط بجينات بول، وبالتالي هناك علاقة جوهرية بين هذا الجين وسرطان الدم النخاعي المزمن (CML) مقارنة بالأشخاص الأصحاء.

الكلمات المفتاحية: HTLV-1 الورم الخبيث، *Pol*، *tax/rex* ، الأورام الخبيثة، مدينة الحلة، سرطان الدم النخاعي المزمن.