ORIGINAL ARTICLE

Human T-lymphotropic virus-1 proviral load among patients on maintenance hemodialysis

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ABSTRACT

Introduction: Human T-lymphotropic virus type 1(HTLV-1) is a complicated leukemogenic retrovirus, it is the first oncogenic virus discovered and identified as the leading cause of T-cell malignancy and HTLV related myelopathy with a long latency period. Transmission via infected blood products is one of the common routes of HTLV-1 infection, and hemodialysis patients are potentially more vulnerable to blood-borne viral infections such as HTLV. This study aimed to determine the factors associated with HTLV-1 proviral load among hemodialysis patients.

Materials and Methods: A cross-sectional study of 130 patients undergoing hemodialysis was conducted between November 2023 and January 2024. After HTLV-1 RNA extraction, complementary DNA (cDNA) was synthesized. HTLV-1 pro-viral load (PVL) was quantified by real-time PCR (qRT-PCR).

Results: HTLV-proviral load was detected in 57 (43.84%) blood samples, with a mean ± standard deviation (SD) of 16.3×103 ± 5.4×104(copies/µL), including 34 (26.2%) males and 23 (17.7%) females. The highest percentage of infection (22.3%) was detected in the 40-59 age group and married patients (39.2%); however, a high viral load was observed in the 20-39 age group. Frequent blood transfusions associated with HTLV-1 infection were observed in 42 patients (32.3%). Myelopathy-related muscle spasms and paresthesia were significantly associated with the HTLV-1 viral load (p<0.05). A statistically significant relationship was observed between asymptomatic patients and high HTLV-1 proviral load (p=0.004).

Conclusion: These findings show that a significant number of dialysis patients were infected with HTLV-1. Therefore, hemodialysis patients should be frequently screened for HTLV-1 infections.

KEYWORDS:
HTLV-1, Hemodialysis, Real-time PCR, Oncovirus, Myelopathy

INTRODUCTION

Human T-lymphotropic virus Type One (HTLV-1) belongs to the Retroviridae family and is classified into the genus Deltaretrovirus.[1] HTLV-I has a genome of positive-sense dimeric single-stranded RNA similar to other retroviruses, which encodes structural and enzymatic proteins such as gag, env, and pol, as well as a unique region at the 3′ end, referred to as the pX region.[2] This indicates the presence of regulatory proteins such as Rex, basic leucine zipper factor (HBZ), and trans-activator protein (Tax).

Globally, approximately 10 to 20 million people are reported to be carriers of HTLV-1, with the virus being more prominent in specific countries such as Japan (2.7%-21.2%), the Caribbean region (up to 6%), Brazil (up to 2%), Northeast Iran (0.6%), Central Africa, and many regions of South America.[3,4]

HTLV-1 transmission in vivo is facilitated by breastfeeding, blood transfusions, needle sharing, and sexual contact.[5,6] Furthermore, HTLV-1 has been shown to spread efficiently in transplant patients.[7] During hemodialysis (HD), the blood is filtered through a dialysis machine. Although this procedure can be effective in treating kidney failure, it also exposes patients to the danger of infectious complications of hemodialysis, including infections caused by contaminated water or equipment, and the transfer of various blood-borne viruses, such as HIV, HTLV, and HCMV.[8,9] Patients undergoing HD are among the highest risk categories for HTLV-1 transmission because they regularly require blood transfusions,[10] and HD patients, as well as those with thalassemia and hemophilia, are more vulnerable to infections acquired through transfusions.[11] The relationship between HTLV-1 transmission and blood transfusion is widely recognized and has been validated in various investigations of blood donors from several countries.[12-14]

Previous research has shown that individuals infected with HTLV-1 have a higher adjusted risk of death from any cause compared to those who are HTLV-1 negative, with a relative risk of 1.57 (95% CI 1.37–1.80).[15] Additionally, these individuals are at increased risk of developing diabetes and chronic kidney disease.[16]

HTLV-1 is a known cause of adult T-cell leukemia (ATL), which develops in 5% of affected individuals, as well as a life-threatening neurological condition, HTLV-1 associated myelopathy/tropical spastic paraparesis (HAM/TSP). Moreover, various inflammatory disorders associated with this infection have been documented, including uveitis, Hashimoto thyroiditis, Graves' disease, pulmonary disease, infective dermatitis, myositis, and arthritis.[17]

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HTLV-1 infection causes continuously elevated levels of proinflammatory cytokines and chemokines systemically[18,19] which have been independently linked to accelerated renal function loss in other cases.[20] A study conducted in Brazil found that 2 out of 15 individuals who tested positive for HTLV (approximately 13.3%) experienced bladder dysfunction. This may be attributed to neurological impairment caused by the virus, which could contribute to the development of end-stage renal disease. However, a definitive clinical link between HTLV infection and this disease has not yet been established.[21]

A recent assessment surveyed the status of hemodialysis patients in Iraq, involving 10,721 cases from all Iraqi governorates. The study found that Baghdad had the highest population of patients undergoing hemodialysis, accounting for 27.0% of the cases. Additionally, 71.8% of the patients received two hemodialysis sessions each week. Hypertension and diabetes mellitus were identified as the primary etiological factors leading to renal disease in these patients, affecting 40.3% and 32.3% of these patients, respectively.[22] Due of the increasing spread of this virus worldwide and limited epidemiological data, this study aimed to investigate HTLV-1 infection in hemodialysis patients and to evaluate the associated factors.

MATERIALS AND METHODS

A cross-sectional study was conducted involving 130 hemodialysis patients of both sexes, aged 18–82 years, who had been undergoing hemodialysis for at least six months due to longstanding, uncontrolled diabetic nephropathy with or without hypertension. Participants were recruited from the Dialysis Center at Al-Imamein Kadhimein Medical City in Baghdad, Iraq, between November 2023 and January 2024. Patients under 18 years of age were excluded from the study, as many declined to participate or had not attended the center regularly. Additionally, HIV-infected patients were not included because HIV can activate HTLV-I viral expression through interactions with host cellular genes, potentially affecting the accuracy of proviral load results.

The Ethics Committee of the Department of Microbiology at the College of Medicine, University of Baghdad approved the research protocol (IRB No. 0230A in November 2023). After being fully informed about the study objectives, all patients signed a consent form for participation.

Each patient was interviewed and data regarding their age, sex, history of chronic diseases, blood transfusion, and details about their dialysis conditions such as vascular access, cause, frequency, and duration of dialysis were collected.

A five-milliliter whole blood sample was taken from each patient aseptically via venipuncture. Four hundred microliters of blood was then mixed with 600 µL of triazole reagent in Eppendorf tubes and stored at -20°C until further use. Sample collection was performed with the consent of all the participating patients.

RNA extraction

HTLV-1 RNA was extracted from each blood sample using the organic method outlined in the TRIzol reagent protocol. Specifically, 0.4 mL of blood was combined with 0.6 mL of TRIzol™ Reagent, and the lysate was homogenized by carefully pipetting up and down several times. To each tube, 0.2 mL of chloroform was then added, and the tube cap was securely fastened. These mixtures were incubated for 2-3 minutes before centrifugation for 10 minutes at 10000 rpm. This process resulted in the separation of the mixture into a lower organic phase, interphase, and colorless upper aqueous phase. The aqueous phase containing the RNA was subsequently transferred to a new tube and stored at -20°C for later analysis. To precipitate total RNA, isopropanol (0.5 mL) was added to the aqueous phase, and the mixture was incubated for an additional 10 min before being centrifuged for 10 min at 12,000 rpm. Finally, the supernatant was discarded, leaving a white gel-like pellet at the tube bottom. The RNA was washed by adding 70% ethanol (0.5 mL), vortexed briefly, and centrifuged for 5 minutes at 10000 rpm.

cDNA synthesis

Complementary DNA (cDNA) was synthesized from an RNA template using OT-1 Reagent Kits (Reverse Transcription Kits), produced by Synthol, Russia. Throughout the procedure, the manufacturer's protocol strictly adhered to each stage of the reaction. cDNA synthesis involved two thermal cycling reactions. In the initial reaction, a random primer and the isolated RNA were subjected to a thermal cycle consisting of 5 min at 70 °C, followed by 10 min at 4°C. The subsequent cDNA reaction was conducted under the following conditions: 15 min at 37 °C, 1 h at 45 °C, and concluded with 5 min at 92 °C. As specified by the manufacturer, the total reaction volume was maintained at 20µL. The concentration of cDNA was quantified using a Quantus Fluorometer, revealing concentration values within the range of 0.054–15 ng/µL.

Real time PCR (RT-PCR)

Quantitative Real-Time PCR (SYBR green assay) was performed using a Mic qPCR Cycler (Bio Molecular System) employing GoTaq qPCR Master Mix (Promega, USA). To detect HTLV-1, primer sequences supplied by (Macrogen/Korea) targeting the virus transactivating gene (Tax gene) were used as follows: forward primer, 5’CCCTAATAATTCTACCCGAGGACTG3’ and reverse primer, 5’GCCATCGGTAAATGTCCAAATAAGG3.’

The procedure was carried out in a reaction volume of 10µl according to the instructions provided by the manufacturer. The thermal cycler reactions were programmed as follows: one cycle of initial denaturation was set at 95°C for 5 min, followed by 40 cycles of denaturation, annealing, extension was set at 95°C for 20 min, 63°C for 20 min, and 72°C for 20 minutes respectively. A standard curve was created using sequential dilutions of the template version number used in the qPCR assay. Linear regression of log concentration (copy µl-1) versus CT gives the standard curve, and proviral load was expressed as HTLV-1 (copy/µL) peripheral blood.

Table I: HTLV-1 viral load in relation to the patients' characteristics

Variables	Positive HTLV-1 No. (%)	Negative HTLV-1 No. (%)	95% confidence interval	Viral load (Copies/µL) Mean ± SD	P-value
Age/year:					
<20	2 (1.5)	1(0.8)		$2.6\times10^3 \pm 3.6\times10^3$	
20-39	8(6.2)	11(8.5)	0.16-0.30	$33.73\times10^4 \pm 8.2\times10^3$	0.63
40-59	29(22.3)	30(23.1)		$11.6\times10^3 \pm 5.6\times10^4$	
≥60	18(13.8)	31(23.8)		$13.6\times10^3 \pm 4.8\times10^4$	
Sex:					
Male	34(26.2)	43(33)	0.19 - 0.34	$13.5\times10^3 \pm 5.6\times10^4$	0.93
Female	23(17.7)	30(23.1)		$20.5\times10^3 \pm 5.2\times10^4$	
Marital status:					
Married	51(39.2)	63(48.5)	0.31-0.47	$6.4\times10^3 \pm 12.2\times10^4$	0.34
Unmarried	6 (4.6)	10 (7.7)		$56.6\times10^3 \pm 13.3\times10^4$	
Diabetes Miletus					
Yes	26(20)	26(20)	0.13 - 0.27	$24.8\times10^2 \pm 3.5\times10^3$	0.82
No	31(23.8)	47(36.2)			
Hypertension					
Yes	46(35.4)	60(46.1)	0.27 - 0.43	$12.6\times10^3 \pm 3.8\times10^4$	0.24
No	11(8.5)	13(10)			
Total No. (%)	57(43.8)	73(56.2)	0.35-0.52	$16.3\times10^3 \pm 5.4\times10^4$	0.8

Table II: HTLV-1 RT-PCR results in relation to hemodialysis risk factors

Risk factor	Positive HTLV-1 NO.(%)	Negative HTLV-1 NO.(%)	95% confidence interval	Viral load (Copies/µL) Mean ± SD	P-value
Frequency of blood transfusion					
Nil	16(12.3)	19(14.6)	0.18 -0.33	$2.78\times10^3 \pm 0.33\times10^4$	0.63
Once	8(6.2)	15(11.5)		$36.66\times10^3 \pm 7.38\times10^4$	
More than two	33(25.4)	39 (30)		$17.92\times10^3 \pm 6.15\times10^4$	
Vascular access					
AV fistula	51(39.23)	64(49.23)	0.31 -0.47	$16.3\times10^3 \pm 5.4\times10^4$	0.74
Double lumen	6(4.62)	9(6.92)		$14.9\times10^3 \pm 4.1\times10^4$	
Frequency of dialysis/week					
Twice	15(11.53)	10(7.7)	0.24 - 0.40	$17.3\times10^3 \pm 5.6\times10^4$	0.07
Three time	42(32.3)	63(48.5)		$10.74\times10^3 \pm 3.5\times10^4$	

Table III: HTLV-1 RT-PCR results in association to myelopathy clinical presentations

*Symptoms	HTLV-1 PCR results		95% confidence interval	P-value
	Positive No. (%)	Negative No. (%)		
Progressive weakness				
Yes	6 (4.6)	11(8.5)	0.02 - 0.09	0.45
No	51(39.2)	62(47.7)		
Muscle spasm				
Yes	49 (37.7)	44(33.8)	0.29 - 0.46	0.001
No	8(6.2)	29(22.3)		
Paresthesia				
Yes	40 (30.8)	38(29.2)	0.23 - 0.39	0.03
No	17(13.1)	35(26.9)		
Asymptomatic				
Yes	5 (3.8)	21(16.2)	0.01-0.08	0.004
No	52(40)	52(40)		

*Patients may experience more than one symptom

Statistical analysis

Data were analyzed using IBM's Statistical Package for the Social Sciences, version 21 (SPSS). Data were compared using Pearson's chi-square (χ^2-test) for the two groups and ANOVA for multiple variables. Statistical significance was set at $p < 0.05$.

RESULTS

Out of the enrolled 130 patients predominantly male (77 males and 53 females) aged 18 to 82 years, the mean age± SD was 51.1 ± 14.8 years. The male-to-female ratio was 1.5:1. HTLV-1 proviral load was identified in 57 (43.8%) patients, with a mean proviral load ±SD of 16.3×103 ± 5.4 ×104, 34 (26.2%) were male and 23 (17.7%) were female. Males were observed to have higher HTLV-1 infection rates. Data obtained from this study revealed that 26 (20%; 95%CI 0.13-

0.27) of diabetic patients were HTLV-1 infected individual, and 46 (35.4%; 95%CI 0.27-0.43) of patients had hypertension. No statistical difference was observed between HTLV-1 viral load and any other chronic disease, as shown in table I.

In this study, 33 patients (25.4%; 95%CI 0.18 -0.33) with a viral load of who received frequent blood transfusions had a positive viral load of 17.92 ×103± 6.15×104 compared to 16 (12.3%) with a viral load of 2.78 ×103± 0.332×104 did not receive any blood. Regarding dialysis vascular access, fifty-one (39.23%;95%CI 0.31-0.47) of patients who were on arteriovenous (AV) fistula showed positive evidence of HTLV-1 infection, while 6 (4.62%) were using double lumen as hemodialysis access; according to the study results, the majority of HTLV-1 positively detected patients were observed in those who underwent hemodialysis three times per week 42(32.3%;95%CI 0.24 - 0.40), as illustrated in Table II.

Human T-lymphotropic virus-related myelopathy was also identified in this study, and the results demonstrated that HTLV-1 was associated with muscle spasm in 49 (37.7%) and paresthesia in 40(30.8%) patients. Significant statistical differences were found in HTLV-1 RT-PCR results ($p<0.05$). A highly significant association of asymptomatic patients with HTLV-1 results was observed with a p-value of 0.004, as shown in Table III.

DISCUSSION

HTLV-1 infection has spread globally, the scarcity of recent epidemiological studies, and the majority of HTLV prevalence data are mainly derived from endemic areas; hence, the real number of HTLV-1 infection rates is probably greater than previously reported.[23] Patients undergoing hemodialysis have a greater risk of infection, which can be attributed to weakened immune systems, frequent hospital stays, and surgeries.

This research is a complementary study to our previous work that focused on the detection of HTLV-1 P24 antigen indicating a significant active antigenemia among hemodialysis patients in 60/130(46.2%) of cases,[24] these findings were almost similar to the present study. Notably, in the current study of HD patients, HTLV viral load was detected in 43.84% of them, indicating a high frequency of infection. There is limited information on HTLV-1 prevalence and its associated diseases in Iraq. However, earlier studies have reported the presence of HTLV-1 in patients with lymphoma and leukemia and among blood donors. HTLV-1 and HTLV-2 were first investigated in patients with leukemia and lymphoma in Iraq between July 2008 and May 2009. The research found that 3 out of 250 patients studied had a positive result, resulting in a prevalence rate of 1.2%.[25] Additionally, in 2015, a study was conducted to screen 15,239 Iraqi blood donors for antibodies to HTLV-1 and HTLV-2 in their serum, using a chemiluminescent microparticle immunoassay for confirmation. The results revealed that Thirty-nine donors tested positive for either HTLV-1 or HTLV-2. Prevalence rates varied by region, with the highest occurrence in Baghdad, where 24 individuals (61.5%) were seropositive. Other regions reported the following positive cases: Karbala, five (12.8%); Al-Qadisiyyah, four (10.2%); Al-Najaf, two (5.1%); Al-Muthanna, two (5.1%); Al-Basrah, one (2.5%); and Wasit province, one (2.5%).[26]

HTLV-1 was more prevalent among individuals aged 40–59 years, suggesting prolonged exposure to the virus. However, high viral loads have been observed at an early age. indicating the possibility of sexual transmission, particularly in those below the age of 40 years. In comparison to the results of a previous study in Iran, HTLV-1 seropositivity was recognized in 20 cases, representing 14.5% of the total, and all positive results were verified by the line immunoassay, 10.5% were males and 19.3% females, and the incidence rate of HTLV-1 infection was significantly higher in older patients aged 65 years or above (25.58%.[27] Moreover, in a cross-sectional study of maintenance hemodialysis (MHD) patients in Brazil, HTLV-1 infection was found to be (2.48% (15/605). The incidence of HTLV-1 infection increased with age, from 1.6% in individuals aged 18 to 30 years to 2.9% in those over 50 years of age. The chance of being positive for HTLV-1 increases by 4% in each year of age. The fact that aging increases exposure to events such as blood transfusions, intravenous drug use, and sexual activity, which can lead to the virus's acquisition, could be one explanation for this association. HTLV-1 requires no known medical treatment. Unfortunately, once the infection is proven, it is passed throughout life.[28] Infection prevention is therefore critical to contain it.

Our findings indicate that males had a higher infection rate than females, with 36.2% of HTLV-1 infected patients being males. Additionally, married patients exhibited a higher percentage of infection than unmarried patients, despite the latter having a higher viral load. This observation contrasts with previous cross-sectional studies among hemodialysis patients, which reported higher rates of HTLV-1 infection in females than in males and unmarried individuals.[29]

In the present study, 33 of 130 hemodialysis (HD) patients (25.4%) who received frequent blood transfusions tested positive for HTLV-1 viral load compared to those who did not receive transfusions. Because of the frequent need for blood transfusions, patients undergoing HD are among the highest risk groups for HTLV-1 infection[10], Previous research has established this relationship, highlighting the potential risk associated with transfusing blood infected with HTLV-1. One study found that the incidence of infection was significantly higher in dialysis patients who had received blood transfusions, with 153 out of 681 (22.5%) testing positive for HTLV-1, than in those who had never received transfusions.[30]

The process of hemodialysis itself involves regular and extended blood exposure through vascular access and the extracorporeal circle, as well as the proximity of other patients during dialysis, interaction with medical personnel, and replacement of dialysis equipment.[31] According to this study, 38.23% of patients with AV fistula were HTLV-1 positive; furthermore, patients who underwent dialysis three times per week experienced the highest rate of infections. Infection is another significant concern that typically involves vascular access[32] as 20 percent of AV fistula complications are caused by infection.[33]

The development of effective and affordable HTLV screening strategies for donated blood samples should be carefully evaluated in prevalent area. Thus, it is likely to have a substantial impact on the occurrence of HTLV-associated diseases. HTLV screening of donated blood has been routinely implemented in Brazil, Canada, the United States, and other countries in the United States. This certainly reduced the incidence of new infections among blood recipients.[34]

Moreover, 20% of HTLV-1 positive hemodialysis patients in the current study had diabetes. The strong relationship between HTLV-1 and long-term inflammation, as well as the connection between this viral life cycle and glucose metabolism, could be responsible for these disease correlations. According to an Australian study, increased HTLV-1 PVL was linked to a two-fold rise in the incidence of diabetes and chronic kidney disease.[17] HTLV-1 virology is inextricably linked to glucose metabolism, and individuals with high HTLV-1 viral load are more likely to develop diabetic comorbidities, including chronic kidney disease. Diabetes was shown to be more common among Australian Aboriginal people in a study of dialysis patients.[34] in vitro, HTLV-1 infection decreased glucose transporter 1 (GLUT-1) expression on the plasma membrane. This was related to inadequate glucose absorption.[35,36]

Most individuals infected with HTLV-I remain asymptomatic carriers throughout their lives, with only 5-10% developing noticeable clinical symptoms. In cases related to human T-lymphotropic virus-associated myelopathy, our findings suggest a close link between HTLV-1 infection and symptoms, such as muscular spasms and paresthesia. Additionally, HTLV-1 triggers a strong inflammatory response in the human body, which may increase the risk of non-communicable diseases. Once infected, the virus causes CCR4+ CD4+ T cells to produce pro-inflammatory cytokines such as interferon-γ, leading to the establishment of a T-helper1 phenotype in vivo. Elevated levels of pro-inflammatory cytokines and chemokines in both the bloodstream and tissues are believed to contribute to organ inflammation, including the central nervous system[17,18] This inflammation is closely correlated with a higher HTLV-1 proviral load in peripheral blood cells.[37,38]

This study has some limitations that are important considerations. A primary limitation of cross-sectional research is that correlations do not imply causation, especially because this study was conducted at a single center. Additionally, the small sample size may have affected the accuracy of the estimates for viral percentages. Nevertheless, the quantification of viral copies using qPCR is highly sensitive and can effectively predict associated diseases. It is important to note that patients with very low proviral loads may give false-negative results; however, these individuals are unlikely to transmit the virus because of their extremely low viremic status.

CONCLUSION

The incidence of HTLV-1 infection in Iraqi hemodialysis patients is significantly high. Therefore, early detection at dialysis centers is critical for minimizing the risk of HTLV-1 infection. Therefore, preventive measures are mandatory for infection control. Furthermore, investigations across various Iraqi cities are recommended for other high-risk populations.

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REFERENCES

1. Simmonds P, Adriaenssens EM, Lefkowitz EJ, Oksanen HM, Siddell SG, Zerbini FM, et al. Changes to virus taxonomy and the ICTV Statutes ratified by the International Committee on Taxonomy of Viruses (2024). Arch Virol 2024; 169(11): 236-48.
2. Franchini G, Tartaglia J, Markham P, Benson J, Fullen J, Wills M, et al. Highly attenuated HTLV type I env poxvirus vaccines induce protection against a cell-associated HTLV type I challenge in rabbits. AIDS Res Hum Retroviruses 1995; 11(2): 307-13.
3. Ghaffari J, Ebrahimi M, Makhlough A, Mohammadjafari H, Nazari Z. Seroepidemiology of human T-cell lymphotropic virus 1 infection in hemodialysis patients: should we be concerned about it? Iran J Kidney Dis 2013; 7: 187-90.
4. Gonzalez-Alcaide G, Ramos JM, Huamani C, MENDOZA Cd, Soriano V. Human T-lymphotropic virus 1 (HTLV-1) and human T-lymphotropic virus 2 (HTLV-2): geographical research trends and collaboration networks (1989-2012). Rev Inst Med Trop Sao Paulo 2016; 58: 11-20.
5. Percher F, Jeannin P, Martin-Latil S, Gessain A, Afonso PV, Vidy-Roche A, et al. Mother-to-child transmission of HTLV-1 epidemiological aspects, mechanisms and determinants of mother-to-child transmission. Viruses 2016; 8(2): 40-9.
6. Lairmore MD, Haines R, Anupam R. Mechanisms of human T-lymphotropic virus type 1 transmission and disease. Curr Opin Virol 2012; 2(4): 474-81.
7. Cook LB, Melamed A, Demontis MA, Laydon DJ, Fox JM, Tosswill JH, et al. Rapid dissemination of human T-lymphotropic virus type 1 during primary infection in transplant recipients. Retrovirology 2016; 13: 1-9.
8. Roushan MRH, Farokhtabar S, Bayani M, Siadati S. Epidemiological aspects of hepatitis B and C and human immunodeficiency viruses among hemodialysis patients in Mazandaran Province, Iran. Nephrourol Mon 2016; 8(3): e37878.
9. Tokars JI, Arduino MJ, Alter MJ. Infection control in hemodialysis units. Infect Dis Clin North Am 2001; 15(3): 797-812.
10. Khameneh ZR, Baradaran M, Sepehrvand N. Survey of the seroprovalence of HTLV I/II in hemodialysis patients and blood donors in Urmia. Saudi J Kidney Dis Transpl 2008; 19(5): 838-41.
11. Eleftheriadis T, Liakopoulos V, Leivaditis K, Antoniadi G, Stefanidis I. Infections in hemodialysis: a concise review. Part II: blood transmitted viral infections. Hippokratia 2011; 15(2): 120-6
12. Hedayati-Moghaddam MR, Tehranian F, Bayati M. Human T-Lymphotropic virus type I (HTLV-1) infection among Iranian blood donors: First case-control study on the risk factors. Viruses 2015; 7(11): 5736-45.
13. Schreiber G, Murphy E, Horton J, Wright D, Garfein R, Chien HC, et al. Risk factors for human T-cell lymphotropic virus types I and II (HTLV-I and-II) in blood donors: the Retrovirus Epidemiology Donor Study. J Acquir Immune Defic Syndr Hum Retrovirol 1997; 14(3): 263-71.
14. O'Brien S, Goldman M, Scalia V, Yi QL, Fan W, Xi G, et al. The epidemiology of human T-cell lymphotropic virus types I and II in Canadian blood donors. Transfus Med 2013; 23(5): 358-66.
15. Martin F, Taylor GP, Jacobson S. Inflammatory manifestations of HTLV-1 and their therapeutic options. Expert Rev Clin Immunol 2014; 10(11): 1531-46.

16. Schierhout G, McGregor S, Gessain A, Einsiedel L, Martinello M, Kaldor J. Association between HTLV-1 infection and adverse health outcomes: a systematic review and meta-analysis of epidemiological studies. Lancet Infect Dis 2020; 20(1): 133-43.
17. Talukder MR, Woodman R, Pham H, Wilson K, Gessain A, Kaldor J, et al. High human T-cell leukemia virus type 1c proviral loads are associated with diabetes and chronic kidney disease: results of a cross-sectional community survey in central Australia. Clin Infect Dis 2023; 76(3): e820-e6.
18. Futsch N, Prates G, Mahieux R, Casseb J, Dutartre H. Cytokine networks dysregulation during HTLV-1 infection and associated diseases. Viruses 2018; 10(12): 691-708.
19. Zargari R, Mahdifar M, Mohammadi A, Vahidi Z, Hassanshahi G, Rafatpanah H. The Role of Chemokines in the Pathogenesis of HTLV-1. Front. Microbiol 2020; 11: 421-37.
20. Amdur RL, Feldman HI, Gupta J, Yang W, Kanetsky P, Shlipak M, et al. Inflammation and progression of CKD: the CRIC study. Clin J Am Soc Nephrol 2016; 11(9): 1546-56.
21. Araujo AQ-C. Update on neurological manifestations of HTLV-1 infection. Curr Infect.Dis Rep 2015; 17: 459-66.
22. Ismael IM, Khalaf AS, Ali DM, Al Saedi AJ. Current status of hemodialysis in Iraq. Iraqi Natl J Med 2025; 7(1): 122-33.
23. Gessain A, Cassar O. Epidemiological Aspects and World Distribution of HTLV-1 Infection. Front. Microbiol 2012; 3: 388-411.
24. Al-jubouri Z, Abdullah SF. Active Human T-lymphotropic Virus Type-1 Antigenemia in a Sample of Iraqi Patients on Maintenance Hemodialysis. AL-Kindy College Medical Journal. 2025;21(1):58-64.
25. Al-Rawi JR, Latief AMA, Abdulkareem S. Screening For HTLV 1 & 2 Among Iraqi Patients With Lymphoma And Leukemia. Iraqi Journal of Community Medicine 2017; 30(4): 165-8.
26. Ibrahim AI, Al-Musawi YA, Abdullah AI. Seroprevalence of HTLV-type-1 and type-2 among Blood Donors in Some Iraqi Provinces. IJFMT 2020; 14(4): 2179-84.
27. Hedayati-Moghaddam MR, Fathimoghadam F, Soghandi L, Darrudi A. High prevalence of HTLV-1 infection among hemodialysis patients in Neyshabur, northeast of Iran. Int J Infect 2019; 6(1): e85164.
28. Santos RF, Conceição GC, Martins MS, Kraychete A, Penalva MA, Carvalho EM, et al. Prevalence and risk factors for Human T-Lymphotropic Virus Type 1 (HTLV-1) among maintenance hemodialysis patients. BMC Nephrol 2017; 18: 1-7.
29. Lee SY, Mastushita K, Machida J, Tajiri M, Yamaguchi K, Takatsuki K. Human T-cell leukemia virus type I infection in hemodialysis patients. Cancer 1987; 60(7): 1474-8.
30. Timofte D, Dragos D, Balcangiu-Stroescu A-E, Tanasescu M-D, Balan DG, Avino A, et al. Infection with hepatitis C virus in hemodialysis patients: An overview of the diagnosis and prevention rules within a hemodialysis center. Exp Ther Med 2020; 20(1): 109-16.
31. Marticorena RM, Dacouris N, Donnelly SM. Randomized pilot study to compare metal needles versus plastic cannulae in the development of complications in hemodialysis access. J Vasc Access 2018; 19(3): 272-82.
32. Saxena AK, Panhotra B, Al-Mulhim AS. Vascular access related infections in hemodialysis patients. Saudi J Kidney Dis Transpl 2005; 16(1): 46-71.
33. Proietti FA, Bárbara F AB, Proietti C. HTLV in the Americas. Rev Panam Salud Publica/Pan Am J Public Health 2006; 19(1): 7-8
34. Talukder MR, Clauss CS, Cherian S, Woodman R, Einsiedel L. Risk factors for HTLV-1, acute kidney injury, and urinary tract infection among aboriginal adults with end stage kidney disease in central Australia. J Med Virol 2021; 93(11): 6362-70.
35. Al-Saleem J, Dirksen WP, Martinez MP, Shkriabai N, Kvaratskhelia M, Ratner L, et al. HTLV-1 Tax-1 interacts with SNX27 to regulate cellular localization of the HTLV-1 receptor molecule, GLUT1. PLoS One 2019; 14(3): e0214059.
36. Kulkarni A, Mateus M, Thinnes CC, McCullagh JS, Schofield CJ, Taylor GP, et al. Glucose metabolism and oxygen availability govern reactivation of the latent human retrovirus HTLV-1. Cell Chem Biol 2017; 24(11): 1377-87.
37. Verdonck K, González E, Van Dooren S, Vandamme A-M, Vanham G, Gotuzzo E. Human T-lymphotropic virus 1: recent knowledge about an ancient infection. Lancet Infect Dis 2007; 7(4): 266-81.
38. Bangham CR, Araujo A, Yamano Y, Taylor GP. HTLV-1-associated myelopathy/tropical spastic paraparesis. Nat Rev Dis Primers 2015; 1(1): 1-17.