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“O HTLV em diferentes grupos populacionais no Estado de Goiás”

08:50-09:10 ALDEMIR BRANCO DE OLIVEIRA FILHO (PA)

“O vírus infotrópico de células T humanas 1 e 2 entre usuários de drogas no Estado do Pará, Norte do Brasil”

09:10-09:35 MARIA FERNANDA RIOS GRASSI (BA)

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09:35 – 10:00 GRAÇA VIANA (MA)

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10:00-10:20 COFFEE BREAK

10:20- 11:00 EDUARDO GOTUZZO HERENCIA (PERU)

“O impacto e evolução da coinfeção HTLV 1 e Strongyloides”

11:00 – 11:40 CHARLES BANGHAM (UK)

“O HTLV-1 altera a estrutura e a transcrição da cromatina do hospedeiro por mutagenese à distância”

11:40- 12:05 ANA CAROLINA DE PAULO VICENTE (RJ)

“Agregação familiar do HTLV”

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14:30 – 15:10 CARLOS CHIATTONE (SP)

“Registro brasileiro de linfomas T”

15:10 – 15:50 JUAN CARLOS RAMOS (USA)

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15:50 – 16:15 PEDRO DANTAS OLIVEIRA (BA)

“Leucemia/linfoma T do adulto: fatores prognósticos e envolvimento cutâneo”

16:15 – 16:40 PAULA LOUREIRO (PE)

“Leucemia/linfoma T do adulto: passado, presente e futuro – situação no mundo e no Brasil”

16:40 – 17:20 EDWARD MURPHY (USA)

“Epidemiologia do HTLV-1 E HTLV- 2: estado da ciência”

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28 de agosto de 2018 - Salão - Karajás

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- 08:45 – 09:00 Apresentação Oral (Prêmio Carlos Maurício)
- 09:00 – 09:25 CASSIUS JOSÉ VITOR DE OLIVEIRA (BA)
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“Doença pulmonar e o vírus linfotrópico de células humanas tipo 1 (HTLV-1)”
- 09:50 – 10:10 COFFER BREAK
- 10:10 – 10:50 CHARLES BANGHAM (UK)
“A regulação da latência in vivo pelo HTLV-1”
- 10:50 – 11:30 GRAHAM TAYLOR (UK)
“Redefinindo o risco individual na doença associada ao HTLV- 1”
- 11:30 – 11:55 JOSÉ ABRAÃO NETO (BA)
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- 14:30 – 14:45 Apresentação Oral (Prêmio Carlos Maurício)
- 14:45 – 15:00 Apresentação Oral (Prêmio Carlos Maurício)
- 15:00 – 15:25 MARIA ALICE F. QUEIROZ (PA)
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- 15:25 – 15:50 AUGUSTO CESAR PENALVA (SP)
“História natural da PET/MAH”
- 15:50 – 16:30 ABELARDO ARAÚJO (RJ)
“Mielopatia associada ao HTLV: uma doença negligenciada”
- 16:30 – 17:10 JORGE CASSEB (SP)
“Bases genéticas para evolução da infecção assintomáticas para o desenvolvimento da PET/MAH”
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29 de agosto de 2018 - Salão - Karajás

PROGRAMAÇÃO

Imunologia e Imunopatologia do HTLV

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09:10 – 09:35 EDEL B. STANCIOLI (MG)

“Análise prospectiva dos níveis de anti-Tax IgG em indivíduos infectados pelo HTLV- 1 na coorte GIPH”

09:35 – 10:00 EDGAR M. CARVALHO (BA)

“Características clínicas e imunológicas entre pessoas infectadas pelo HTLV-1 com carga viral alta ou baixa”

10:00 – 10:20 COFFEE - BREAK

10:20 – 11:00 GLEN BARBER (USA)

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11:00 – 11:40 JOHAN VAN WEYENBERGH (BÉLGICA)

“Uma perspectiva genômica e evolucionária na apoptose, proliferação e inflamação nas patologias associadas ao HTLV-1”

11:40 – 12:05 HELLEN T. FUZII (PA)

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12:05 – 14:00 INTERVALO –ALMOÇO

Diagnóstico, Prevenção e Controle do HTLV

13:30 – 14:30 Apresentação Pôster

14:30 - 14:50 SANDRA DO VALLE (RJ)

“Desafios das associações de portadores de HTLV no Brasil”

14:50 – 15:10 DEBORAH CRESPO (PA)

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15:10 – 15:35 FILIPE DE BARROS PERINI (DF)

“HTLV: estratégias para seu enfrentamento”

15:35 – 16:00 BERNARDO GALVÃO (BA)

“Um atendimento de saúde integrado e multidisciplinar é de suma importância para as pessoas que vivem com HTLV”

“Estratégias para o desenvolvimento de moléculas teranósticas para o diagnóstico e terapêutica do HTLV-1”

16:40 – 17:20 ADELE CATERINO DE ARAÚJO (SP)

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17:20 – 17:40 RICARDO ISHAK (PA)

“HTLV: onde estaremos em 10 anos?”

17:40 PREMIAÇÕES E ENCERRAMENTO

27 August 2018 - KARAJÁS HALL

PROGRAM

HTLV Biology and Molecular Epidemiology

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“HTLV among different population groups in the State of Goiás“

8:50 - 9:10 ALDEMIR BRANCO DE OLIVEIRA FILHO (PA)

“Human T-cell lymphotropic virus types 1 and 2 among illicit drug users in the State of Pará, Northern Brazil”.

9:10 - 9:35 MARIA FERNANDA RIOS GRASSI (BA)

“Evidence of new endemic clusters of Human T-cell lymphotropic virus in Bahia State, Brazil”

9:35 - 10:00 GRAÇA VIANA (MA)

“Epidemiology of HTLV in the world, in Brazil and in the State of Maranhão”

10:00 - 10:20 COFFEE BREAK

10:20 - 11:00 EDUARDO GOTUZZO HERENCIA (Peru)

“The impact and evolution of the coinfection HTLV-1 and Strongiloides”

11:00 - 11:40 CHARLES BANGHAM (UK)

“HTLV-1 alters host chromatin structure and transcription: distant insertional mutagenesis”

11:40 - 12:05 ANA CAROLINA DE PAULO VICENTE (RJ)

“Family aggregation of HTLV infections”

12:05 - 14:00 LUNCH BREAK.

Epidemiology and Hematological Manifestations of HTLV

13:30 - 14:30 Poster Presentations

14:30 - 15:10 CARLOS CHIATTONE (SP)

“The Brazilian registrar of T lymphomas”

15:10 - 15:50 JUAN CARLOS RAMOS (USA)

“Emerging new therapies targeting adult T-cell leukemia-lymphoma”

15:50 - 16:15 PEDRO DANTAS OLIVEIRA (BA) “

“Adult T-cell leukemia-lymphoma: prognostic factors and skin disorders“

16:15 - 16:40 PAULA LOUREIRO (PE)

“Adult T-cell leukemia-lymphoma: past, present and future – situation in the world and in Brazil”

16:40 - 17:20 EDWARD MURPHY (USA)

“Epidemiology of HTLV-1 and HTLV-2: state of the science”

17:20 - 17:45 MÁISA DA SILVA SOUSA (PA)

“Ten years of monitoring of HTLV infection in university extension activities in Belém, Pará”

18:00 OPENING CEREMONY & COCKTAIL

28 August 2018 - KARAJÁS HALL

PROGRAM

Clinical Manifestations and Treatment

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8:45 - 9:00 Oral presentation (Carlos Mauricio Award)

9:00 - 9:25 CASSIUS JOSÉ VITOR DE OLIVEIRA (BA)
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9:25 - 9:50 JUAREZ ANTONIO SIMÕES QUARESMA (PA)
“Human T lymphotropic virus type 1 and pulmonary diseases”

9:50 - 10:10 COFFEE-BREAK

10:10 - 10:50 CHARLES BANGHAM (UK)
“Regulation of HTLV-1 latency in vivo”

10:50 - 11:30 GRAHAM TAYLOR (UK)
“Redefining the individual risk of HTLV-1-associated disease”

11:30 - 11:55 JOSÉ ABRAÃO NETO
“Etiology, sintomatology and treatment of urinary disfunctions associated to HTLV infection”

12:00 - 14:00 LUNCH BREAK

Neurological Manifestations and Treatment

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14:30 - 14:45 Oral presentation (Carlos Mauricio Award)

14:45 - 15:00 Oral presentation (Carlos Mauricio Award)

15:00 - 15:25 MARIA ALICE F QUEIROZ (PA)
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15:25 - 15:50 AUGUSTO CESAR PENALVA (SP)
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15:50 - 16:30 ABELARDO ARAÚJO (RJ)
“Mielopatya associated to HTLV: a neglected disease”

16:30 - 17:10 JORGE CASSEB (SP)
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17:10 - 17:35 LUIZ CLAUDIO FERREIRA ROMANELLI (MG)
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29 August 2018 KARAJÁS HALL

PROGRAM

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8:50 - 9:10 ANSELMO SOUZA (BA)

“Co-infection HTLV-1 and tuberculosis: clinical, epidemiologic and immunologic aspects”

9:10 - 9:35 EDEL B. STANCIOLI (MG)

“Prospective analysis of IgG anti-Tax levels in HTLV-1 infected individuals from GIPH cohort”

9:35 - 10:00 EDGAR M. CARVALHO (BA)

“Clinic and Immunologic features in HTLV-1 infected subjects with high or low proviral load”

10:00 - 10:20 COFFEE-BREAK

10:20 - 11:00 GLEN BARBER (USA)

“The role of STING in the pathogenesis of HTLV-1 associated disease”

11:00 - 11:40 JOHAN VAN WEYENBERGH (BELGIUM)

“A genome-wide and evolutionary perspective on apoptosis, proliferation and inflammation in HTLV-1-associated pathologies”

11:40 - 12:05 HELLEN T. FUZII (PA)

“The immunological response to HTLV-1”

12:05 - 14:00 LUNCH BREAK

Diagnosis, Prevention and Control of HTLV

13:30 - 14:30 Poster Presentation

14:30 - 14:50 SANDRA DO VALLE (RJ)

“Challenges for the HTLV patient’s associations in Brazil”

14:50 - 15:10 DEBORAH CRESPO (PA)

“Positive actions of the State Health authority of Para to reduce the impact of HTLV”

15:10 - 15:35 FILIPE DE BARROS PERINI (DF)

“Strategies to face the spread of HTLV”

15:35 - 16:00 BERNARDO GALVÃO (BA)

“An integrated and multidisciplinary health care is of paramount importance for the people living with HTLV”

16:00 - 16:40 LUIZ RICARDO GOULART (MG)

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16:40 - 17:20 ADELE CATERINO DE ARAÚJO (SP)

“Surveillance of HIV-1/HTLV-1 and HIV-1/HTLV-2 co-infections in São Paulo, Brazil”

17:20 - 17:40 RICARDO ISHAK (PA)

“HTLV: what is the future for the next 10 years? “

17:40 AWARDS ANNOUNCEMENT / CLOSING CEREMONY

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ACTING OF NURSE IN CARE OF PREGNANTS INFECTED HTLV-1 AND HTLV-2.

Silva, C.A.C; Garcia, C.P.C; Silva, A.N.

Escola Bahiana de Medicina e Saúde Pública.
camlaenf08@gmail.com

The Lymphotropic Virus of the T-cell in human type 1 (HTLV-1) was the first human retrovirus described. The HTLV-2, Lymphotropic Virus of the T-cell in human type 2 was identified in 1982. The prevalence of HTLV-1 in Brazil is diversified and keeps relationship with both the geographic region and the group analyzed. A population study carried out in Salvador has detected prevalence of 1.76%, in addition to higher prevalence in women and its association with lower levels of schooling and income. As the most frequent vertical transmission of HTLV-1 is breast feeding and considering the higher prevalence in women, it is very important the warranty and fulfillment of screening tests for HTLV-1 and 2 as part of the prenatal. These individuals maintain a network of silent transmission, that way, the nurse together with the multidisciplinary team has a key role in the levels of prevalence of vertical transmission. This study has as general goal to describe the performance of the nurse in the care of pregnant women infected by the HTLV-1 and 2, and specific, identify complications in pregnant women infected by the HTLV-1 and 2. This is a narrative bibliographic study whose methodological trajectory is based on the readings, exploratory and selective of the material from the bibliographic search, with search databases: (SCIELO), (LILACS), indexed in the Virtual Health Library (VHL), through the descriptors, HTLV I, HTLV II, and Pregnants. Given the exposed, the professional nurse, along with multidisciplinary team, performs an important role in prenatal care, childbirth and the puerperium, it is in the early discovery of infection by HTLV-1 and 2, screening of this vulnerable population and family for guidance and referrals for assitencial network, impacting in this way on the high levels of vertical transmission.

KEY WORDS: Performance; nurse; care; pregnant; infected; HTLV– 1 and 2.

EPIDEMIOLOGICAL ASPECTS OF HTLV-1/2 INFECTIONS AMONG FEMALE SEX WORKERS IN THE MARAJÓ ARCHIPELAGO, NORTHERN BRAZIL.

Souza, A.P.C; Araújo, A.P.S; Gomes, C.M.; Pinheiro, L.M.L.; Frade, P.C.R; Martins, L.C.; Vallinoto, A.C.R; Ishak, R.; Lemos, J.A.R.; Oliveira-Filho, A.B.

Universidade Federal Do Pará.
pollimed@bol.com.br

Introduction: Female sex workers (FSWs) are highly vulnerable to sexually transmitted infections due to a combination of their sexual behaviour and socioeconomic conditions. The epidemiological situation of human T-lymphotropic virus (HTLV)-1/2 among FSWs is still unknown in northern Brazil. Objectives: To determine the prevalence and factors associated with HTLV-1/2 infections among FSWs in the Marajó Archipelago, as well as to identify the distribution of viral subtypes. Methods: In 2015-2016, biological samples and information were provided by 153 FSWs in municipalities and riverside communities in Marajó Archipelago, northern Brazil. All samples were tested using EIA and real-time PCR. Viral subtypes and subgroups were identified by nucleotide sequencing and phylogenetic analysis. Several variables were analyzed with HTLV-1/2 seropositivity status to identify risk factors for viral infections. Results: Most FSWs were single, heterosexual, less than 30 years, reduced education and born in Pará. In 153 FSWs, 14 (9.15%) had anti-HTLV-1/2 antibodies, and 8 (5.23%) had proviral DNA. Subtypes 1a (n=4), 2c (n=3) and 3b (n=1) were detected. Use of illicit drugs and unprotected sex were associated with viral infections. Conclusions: Epidemiological information on HTLV-1/2 infections in FSWs has been described, and can direct strategies for prevention, control and health promotion.

Financial support: FAPESPA

EPIDEMIOLOGICAL PROFILE OF HTLV PATIENTS OF THE REFERENCE INSTITUTE IN INFECTIOUS DISEASES, RIO DE JANEIRO, BRAZIL.

Hennington, E.A.; Rezende, F.A.V.S.; Pinto, M.L.R.; Leite, A.C.C.B.; Garcia, I.F.S.; Valle, S.C.; Silva, A.R.L.G.; Leal, M.C.; Martins, S.C.S.

Oswaldo Cruz Foundation, Rio de Janeiro, Brazil
ana.leite@ini.fiocruz.br

Brazil has probably the highest absolute number of individuals infected by HTLV, with prevalences varying from 750,000 to 2.5 million. Lack of official data and little investment in epidemiological research contribute to the health and social invisibility of the problem. Objective: To know the epidemiological profile of HTLV patients attending a reference center in infectious diseases. Method: Descriptive epidemiological study based on electronic medical record analysis. Medical records of the HTLV infected cohort, ICD Z22.6 and G04.1 were selected. Results: Of the 977 records, 108 were subsequently identified as deceased, 391 were inactive (patients who have not attended for two years or more), and 478 were active. Of the total number of active patients, the majority were women (58%), over 60 years old (51%), 46% were white, 52% black, and 48% had elementary school. Fifty-six percent were residents of the city of Rio de Janeiro, although many live in the Baixada Fluminense (Rio's urban perimeter) (26%). Among the identified morbidities, most were inserted in chapters I, VI, V, IV and XIII of ICD 10, representing 75% of the diagnoses. Inactive records were 40%, which may characterize abandonment of follow-up. Conclusions: There were problems in the quality of registration of variables such as family income, occupation and religion, and absence of variables of interest such as employment and social security, condom use, alcohol and drug use. New studies should be implemented to broaden and deepen the knowledge about the users being followed and the reasons for abandonment of follow up.

HTLV-1 INTRAFAMILIAL TRANSMISSION AMONG JAPANESE IMMIGRANTS IN BRAZIL.

Bandeira, L.M.; Uehara, S.N.O.; Puga, M.A.M.; Rezende, G.R.; Domingos, J.A.; Vicente, A.C.P.; Lago, B.V.; Niel, C.; Castro, A.R.C.M.

Universidade Federal de Mato Grosso do Sul.
larissa_m_bandeira@hotmail.com

Human T-lymphotropic virus type 1 (HTLV-1) is the etiological agent of adult T-cell leukemia/lymphoma and HTLV-1-associated myelopathy/tropical spastic paraparesis (HAM/TSP). Objectives: The aim of this study was to investigate the intrafamilial transmission of HTLV-1 among Japanese immigrants and their descendants living in a non-endemic area of central Brazil.

Methods: Six families were investigated. Thirty-seven relatives of the six index cases were tested by ELISA for the presence of anti-HTLV antibodies, and the positive cases were confirmed by Western blot. HTLV-1 isolates were genotyped by partial nucleotide sequencing (5' LTR) of the proviral DNA. Results: All individuals, including index cases and relatives, were asymptomatic. In five families, at least one relative was infected with HTLV-1. In all, eight (22%) relatives (one mother, four wives, one brother, and two brothers-in-law) were infected. However, none of the 22 individuals under 55 years of age was infected. In each family, the HTLV-1 sequences from the relatives were identical or almost identical to that of the index case, except in one case. Conclusion: Pedigrees of the families, together with socio-demographic data of the HTLV-1 infected individuals, strongly suggested the occurrence of both vertical and sexual transmission, with breastfeeding as an important risk factor. Whether and why the virus transmission is less effective among younger generations deserves to be further investigated.

HTLV INFECTION AMONG OKINAWAN IMMIGRANTS AND THEIR DESCENDANTS LIVING IN SÃO PAULO.

Bandeira, L.M.; Uehara, S.N.O.; Puga, M.A.M.; Rezende, G.R.; Weis, S.M.S.; Tanaka, T.S.O.; Cesar, G.A.; Domingos, J.A.; Nukui, Y.; Yamashiro, J.; Casseb, J.; Segurado, A.A.C.; Vicente, A.C.P.; Saito, M.O.; Motta-Castro, A.R.C.

Universidade Federal de Mato Grosso do Sul.
larissa_m_bandeira@hotmail.com

The retrovirus Human T-lymphotropic virus (HTLV) is associated with many serious diseases, including adult T-cell leukemia/lymphoma (ATLL) and HTLV-1 associated myelopathy/tropical spastic paraparesis (HAM/TSP). The reported endemic areas for this infection are Central and South America, Caribbean islands, Sub-Saharan Africa, Melanesia, the Middle East and Southwestern Japan. The population of Okinawan immigrants and their descendants is considered vulnerable to HTLV infection because the Okinawa region in Japan is one of the endemic areas of this infection. The world's largest community of Japanese descendants outside of Japan is located in São Paulo, southeast Brazil.

Objectives: This cross-sectional study investigated the prevalence of HTLV infection among Okinawan immigrants and their descendants living in São Paulo.

Methods: After written informed consent, a total of 2,138 volunteer individuals from the five major Okinawa Associations in the state of São Paulo (Casa Verde, Vila Carrão, Ipiranga, Santo André and Liberdade) were interviewed and tested for detection of antibodies against HTLV-1/2 using immunoassay ELISA, between July and August, 2017. New blood samples were collected from all of the individuals who tested positive for anti-HTLV-1/2 and submitted for confirmed by immunoblot assay. In order to provide medical care assistance and individual counseling, patients with HTLV-1 infection and their family members were referred to HTLV Ambulatory of the Hospital das Clínicas-FMUSP.

Results: Among studied population, 59.4% were female, 49.2% had 57 years of age or older and 14.2% were born in Japan. A frequency of 20.5%, 33.3%, 14.2%, 15.6% and 16.2% of the studied population were from Casa Verde, Vila Carrão, Ipiranga, Santo André and Liberdade Associations, respectively. The prevalence of 5.1% (IC 95%: 4.2-6.0) of HTLV-1 infection was found. Of those infected, the majority remain asymptomatic. Molecular analysis of the viral isolates in this population will be carried out as well as the detection of the proviral load of infected individuals.

Conclusion and perspectives: This study revealed a high prevalence of HTLV-1 infection among this Japanese community highlight the need to step up preventive efforts against this infection and more attention given to HTLV-related diseases in this population.

HUMAN T-CELL LYMPHOTROPIC VIRUS TYPES 1 AND 2 AMONG ILLICIT DRUG USERS IN THE STATE OF PARÁ, NORTHERN BRAZIL.

Araújo, A.P.S.; Souza, A.P.C.; Sousa, C.F.; Gomes, C.M.; Martins, L.C.; Vallinoto, A.C.R.; Ishak, R.; Lemos, J.A.R.; Fischer, B.; Oliveira-Filho, A.B.

Institute of Coastal Studies, Federal University of Pará, Bragança. aldbranco@yahoo.com.br

Users of illicit drugs (DUs) are considered an important group of vulnerable due to diverse behaviors who facilitate the acquisition and spread of pathogens. Barriers to access to social and health promotion services, involvement with illicit activities, and stigma are factors that can enhance this vulnerability. In northern Brazil, there are reports of the presence of infection with human T-lymphotropic virus 1 and 2 (HTLV-1 and HTLV-2) in distinct populations, but the epidemiological status of these infections among DUs is still unknown. This study evaluated the prevalence of infection with HTLV-1 and HTLV-2 among DUs in the state of Pará, northern Brazil. **Methods.** This cross-sectional study used the snowball sampling, and obtained biological samples and information from 826 DUs in 28 municipalities in the state of Pará. The samples were screened for the presence of anti-HTLV antibodies using an enzyme-linked immunosorbent assay (ELISA). Viral infections were detailed using real-time polymerase chain reaction (PCR) and nucleotide sequencing. Viral subtypes were identified using Bayesian and maximum likelihood analyzes. Logistic regressions were used to establish the risk factors associated with HTLV-1/2 seropositivity status. **Results.** Most DUs were young, male and had used more than one illicit drug in their lifetime. Crack was the main drug consumed. All users reported using preferably non-injected illicit drugs. However, 111 (13.4%) DUs reported having used injecting drug at least once in their lifetime. The prevalence of antibodies against HTLV-1 and HTLV-2 was 7.6%. The presence of proviral HTLV DNA was detected in 44 DUs (25 with HTLV-1 and 19 with HTLV-2). HTLV-1 isolates belonged to Cosmopolitan subtype I (1a), transcontinental (52.3%) and Japanese (4.5%) subgroups. HTLV-2 isolates belonged to two subtypes: 2b (13.7%) and 2c (29.5%). Injection drug use, drug use greater than three years, unprotected sex, sexual intercourse with another user, and more than 10 sexual partners in the last 12 months were associated with HTLV-1/2 infections. **Conclusion.** This study identified relevant information on HTLV-1/2 infections among DUs in Pará, indicating the need for strategies for control, care and prevention of viral infections in this population.

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KIR3DS1 PROTECTIVE EFFECT AGAINST HTLV-1 INFECTION INFERRED BY WORLDWIDE DATA ANALYSIS.

Ferreira, S.N.; dos Santos, E.F.; Leite, M.M.; da Silva, A.L.S.; dos Santos, E.J.M.

Human and Medical Genetics, Federal University of Pará, Brazil.
samilanatianeferreira@gmail.com

Human T-Cell lymphotropic virus type-1 (HTLV-1) infects mostly T CD4+ lymphocytes, being associated with diseases, like T cell lymphomas/leukemia and tropical spastic paraparesis. Despite the role of killer immunoglobulin-like receptors (KIRs) of natural killer cells in immune response against viral infection, the few case-control studies approaching the influence of KIR in HTLV-1 infection are not consensual. Our aim is to compare the frequencies of 16 KIR genes between two groups the population (total of 93 populations), one with high prevalence and another with low prevalence. The data on HTLV-1 prevalence and KIR frequencies they were obtained for databases <https://ecdc.europa.eu> and www.allelefreqencies.net, respectively. The comparisons were performed by Mann-Whiney test. Only KIR3DS1 ($p=0,0057$) was associated with low prevalence of HTLV-1. This association was not yet reported but the lack of consensus in literature suggests that biases could introduced by demographic factors like migration and admixture. Our study is based on an alternative approach and show a trend free of such bias. Moreover, KIR3DS1 seems to be functionally relevant for antiviral response, since it has been associated with other infections, like HIV, HCV and HBV.

LATE AND EARLY MEMORY IMPAIRMENT: ONE OF THE FIRST SYMPTOMS OF INTERMEDIATE CLINICAL SYNDROME IN HTLV-1-INFECTED CASES.

Gascon, M.R.P.; Haziot, M.E.; Assone, T.; Smid, J.; de Oliveira, A.C.P.; Casseb, J.

Hospital das Clinicas da Faculdade de Medicina de São Paulo.
mariaritapolo@yahoo.com.br

Background: Although classical HAM/TSP syndrome is the most commonly attributed neurological disorder, some “minor” neurological disorders are seen as considerer “asymptomatic” HTLV-1 carriers. These disorders, including cognitive alterations, already observed in descriptions of clinical cases and studies, may constitute an intermediate clinical syndrome (SI). The aim of this study was to investigate the presence of cognitive deficits in patients with HTLV-1 diagnosed as asymptomatic in the first visit to clinic. Method: A total of 79 people were evaluated, 35 of them asymptomatic, 19 with minor neurological alterations (evaluated by a neurologist) and 25 with negative HTLV-1. The instruments used were: Beck’s Depression Inventory, Lawton’s Daily Life Activity Scale, and a complete neuropsychological battery. This evaluation was performed blindly. Results: The majority of participants were female (72.21%), mean age was 52.34 years (SD = 14.29) and average schooling was 9.70 years (SD = 4.11). It was possible to observe those with SI presented lower scores when compared with asymptomatic and control group, relation to auditory episodic memory of immediate recall ($p < 0.01$) and late ($p = 0.01$). Conclusion: Patients with SI presented memory impairment when compared to the other groups. It could be one of the criteria to classified the intermediate syndrome.

PREVALENCE OF HUMAN T-LYMPHOTROPIC VIRUS TYPE 1 AND 2 AMONG INDIGENOUS POPULATIONS IN THE AMAZON REGION OF BRAZIL: A SYSTEMATIC REVIEW OF THE LITERATURE.

Santos, A.A.B.S.; Teixeira, J.C.; Vieira, G.P.; Laurentino, R.V.

Universidade da Amazônia (UNAMA)
amandabastos400@gmail.com

1. Introduction: The Human T-Lymphotropic Virus (HTLV) was the first retroviruses described, existing the type HTLV-1 and 2, however, in the indigenous population the HTLV-2 is more prevalent. 2. Objectives: To perform a systematic review of the literature related to the prevalence of HTLV among indigenous populations in the Amazon region of Brazil. 3. Methods: This study is a qualitative review of the literature, aiming to describe the main characteristics of HTLV, and to speculate on how it arrived in the Amazon region, and verify the determinants that contribute to the prevalence in the indigenous community. 4. Results: Some studies estimated the prevalence of HTLV-1 ranging from 0.48% to 13.9% in the communities of Xicrin, Mekranoiti, Tiriyo, Yanomami, Galibi, Wayampi and Kayapó. The prevalence of HTLV-2, was higher (57.9%), in the communities of Kayapo, Tiriyo, Xicrin, Kraho, Arara Laranjal, Mundukuru, Guarani, Yamamadi, Karitiana, Yanomami, Parakanã, Galibi, Wayana-Apalai, Cinta Larga, and Wayampi. 5. Conclusion: Hypothetically, HTLV-2 was disseminated in indigenous groups in Brazil via the Bering's Strait. The transmission occurs through sexual, vertical and blood contact. Factors that contribute to endemicity in these areas are lack of information, geographical challenges, poor access to communities, less investments efforts in public health policies. Key words: Prevalence, HTLV-1 and 2, Indians Populations, Amazon

CYTOKINES AND CHEMOKINES PROFILES DETECTED IN PLASMA SAMPLES AND CD4+ T CELLS COUNT AND HIV VIRAL LOAD IN HIV-INFECTED AND HCV-, HTLV-1- OR HTLV-2-COINFECTED PATIENTS.

Campos, K.R.; Rigato, P.O.; Oliveira, L.M.S.; Caterino-de-Araujo, A.

Instituto Adolfo Lutz.

karol_rodriguescamp@yahoo.com.br

HIV, HTLV-1/2 and HCV share routes of transmission, and co-infections of such viruses account for worse outcomes of subsequent diseases, except in HIV/HTLV-2. Objective: To quantify cytokines and chemokines in plasma samples from HIV-infected and HIV/HCV-, HIV/HTLV-1- and HIV/HTLV-2-coinfected individuals for identifying profiles that differentiate these co-infections, useful for prognosis. Method: Plasma samples from 129 HIV-infected individuals, matched for age and sex, were divided into six groups: G1 (9 HIV/HTLV-1), G2 (19 HIV/HCV/HTLV-1), G3 (69 HIV), G4 (11 HIV/HCV), G5 (6 HIV/HTLV-2) and G6 (15 HIV/HCV/HTLV-2). They were analyzed by Cytometric Bead Array tests: human Th1/Th2/Th17, human Chemokine and Flex sets (MIP1-a, MIP1-b, and IL1-b). Fluorescence was quantified by flow cytometer LSR FORTESSA, and the data analyzed by FCAP Array 3.0 (all from BD™). Values of CD4+ cells and HIV viral load were collected from medical records. All of patients were HIV+ since the 1980s. Results: Eight cytokines and chemokines could be compared among groups. High levels of Th1 cytokines were detected in G1 (IFN-g) and G6 (IL-6 and IL1-b), and elevated chemokines in G3 (MIG, IP10, RANTES), G4 (MCP1) and G6 (MIP1-b). The highest number of CD4+ cells and the lowest HIV load were detected in HIV/HTLV-2-coinfected patients. Lowest number of CD4+ cells was found among HIV/HTLV-1-coinfected patients. Conclusion: HTLV induced mostly the production of proinflammatory cytokines, and HIV and HCV mainly the chemokines. The obtained results confirmed the worse HIV outcome in HIV/HTLV-1-coinfected patients and for the first time in Brazil, the “protective role” of HTLV-2 in HIV disease progression.

DERMATOLOGICAL MANIFESTATIONS IN PATIENTS WITH HUMAN T-CELL LYMPHOTROPIC VIRUS AT A REFERENCE SERVICE IN AMAZON.

Lobato, B.A.L.; Santos, L.V.; Oliveira, T.R.; Dias, A.L; da Costa, C.A.; Sousa, R.C.M.; de Sousa, M.S.; Xavier, M.B.

Universidade do Estado do Pará.
drabrenaandrade@gmail.com

Individuals infected with HTLV-1 commonly present skin lesions, which may be a warning sign for its diagnosis. Objective: This study describes the most prevalent skin manifestations in HTLV carriers attended at Núcleo de Medicina Tropical (NMT) in Belém-PA. Methods: This is a series of cases study of patients infected with HTLV-1/2 treated at NMT between 1999 and 2016. A descriptive analysis of data was applied. Results: Among 788 surveyed medical records in the service, 15,10% (n = 119) were referred to the dermatology clinic. From the cases that presented skin lesions, 66,39% were female and 33,61% male, the average age was 48 years, predominated patients with noninfectious inflammatory manifestations (64,2%), followed by infectious ones (24,6%) and 1,58% lymphoproliferative diseases. As for the group of lesions, 45,26% of the erythematous-squamous type were observed, followed by dyschromia (24,21%) and eczematous (14,74%). One patient with mycosis fungoides, another with Parapsoriasis and four with infective dermatitis are highlighted. Conclusion: Skin disorders in the HTLV-positive patient are important causes of referral to the dermatologist with etiological and skin lesions groups diversity. In the series of cases studied, lymphoproliferatives diseases and infective dermatitis were a challenge for the diagnosis and clinical management of these patients.

SURVEILLANCE AND MOLECULAR CHARACTERIZATION OF HTLV-2 IN HIV-COINFECTED INDIVIDUALS FROM SÃO PAULO, BRAZIL.

Campos, K.R.; Magri, M.C.; de Araujo, A.C.

Instituto Adolfo Lutz.

karol_rodriguescamp@yahoo.com.br

HTLV-2 is prevalent in Brazil among Amerindians and intravenous drug users (IDU), with or without HIV-1 infection. Four subtypes of HTLV-2 (HTLV-2a to HTLV-2d) were detected in different regions and populations worldwide. Surveillance of the subtypes was important because the routes of retrovirus transmission change with the time. Objectives: Molecular characterization of HTLV-2 in HIV-HTLV-2-coinfected patients from São Paulo, comparing with those from previous years. And to search for the defective particles and mutations that could define the Brazilian signatures of epidemiological and prognostic values. Methods: Sequencing LTR, env and tax segments of HTLV-2 provirus in 35 DNA samples from HIV/HTLV-2-coinfected individuals (all being HTLV asymptomatic) from São Paulo. The Sanger method and the protocols established by Magri et al, 2010 and 2013, were employed. Results and Conclusions: HTLV-2a subtype (variant -2c) was confirmed in all of analyzed samples, except in one (HTLV-2b). The presence of the stop codon in position 8203 in the tax region of HTLV-2 provirus confirmed the extended Tax, characteristic of the Brazilian isolates (Tax2c). Two clusters inside HTLV-2a subtype in phylogenetic trees were detected, associated with the virus transmission/acquisition routes (sexual and IDU), the same overall results were detected in previous years. Defective particles in LTR, tax e env regions were found in 28.6 %, 20.0 % and 8.6 % of sequences, respectively, but it meaning remains to be determined. Molecular signatures characteristic of Brazilian isolates were detected in env, tax and LTR segments. Because of the constant global arrival of immigrants and refugees looking for asylum in Brazil, the continuous surveillance of HTLV-2 is important in this country.

SURVEILLANCE OF HTLV-1 SUBTYPE AND MOLECULAR CHARACTERIZATION OF HTLV-1 IN HTLV-1-MONO- AND HIV/HTLV-1-COINFECTED PATIENTS.

Campos, K.R.; Magri, M.C.; de Moura, P.M.M.F.; de Araujo, A.C.

Instituto Adolfo Lutz.

karol_rodriguescamp@yahoo.com.br

HTLV-1 has a worldwide distribution and its molecular characterization is capable of generating a great amount of information on the origin, geographic region, and dispersion of virus, and also they can be used as markers of prognostic value. Surveillance of HTLV-1 subtypes in HIV/HTLV-1-coinfected patients is important because of the changes in transmission routes of both viruses with time, and the constant arrival of immigrants and refugees in Brazil. Objectives: Molecular characterization of HTLV-1 in HIV-HTLV-1-coinfected patients comparing with those of HTLV-1-monoinfected patients, and to search for mutations and defective particles that could have prognostic value, such as 5'LTR deletion in ATL patients. Methods: Sequencing of LTR, env and tax segments of HTLV-1 provirus in 89 DNA samples, being 63 from HIV/HTLV-1-coinfected individuals from São Paulo (all HTLV-1 asymptomatic), and 26 from HTLV-1-monoinfected patients from Recife (15 asymptomatic, 4 oligosymptomatic, and 7 with HAM/TSP). The Sanger method and the protocols established by Magri et al, 2012 were employed. Phylogenetic trees were constructed, and the sequence mutations, deletions and insertions were searched for the three regions. Results and Conclusions: The HTLV-1aA cosmopolitan subtype, transcontinental subgroup was detected in all of analyzed samples, and the presence of molecular signature characteristic of the Brazilian isolates in the taxA in 86.5 % of samples. Two clusters A and B were identified in phylogenetic trees, confirming the multiple entrances of this virus in both populations. No case of defective particles in 5'LTR segment was detected in HTLV-1-monoinfected patients, contrasting with 38.1 % detected in HIV/HTLV-1 co-infected patients, suggesting interference among these retroviruses. No case of ATL was found in these patients.

DENTAL CARE OF PATIENTS INFECTED WITH HTLV.

Gatinho, J.J.M.; de Sousa, T.C.V.; Oliveira, J.A.A.; Gatinho, M.M.M..

Universidade Federal do Pará.
milagatinho@gmail.com

It's estimated that 15 to 20 million of people in the world are infected by HTLV, being it considered endemic in Brazil. The present study aims to review oral manifestations related to HTLV infection and encourage scientific debates about dental care of infected patients. A literature review was done using the keywords: "HTLV", "Human T-lymphotropic virus 1", "Human T-lymphotropic virus 2", "Dental care", "HTLV infection", that were searched in both English and Portuguese, on the PubMed, Scholar Google and LILACS databases. The most associated to HTLV diseases are TSP/HAM, causing spastic paraparesis, and ATLL. The only oral manifestation of HTLV is Adult T-cell leukemia/lymphoma, being also Sjögren Syndrome mentioned by severe authors and causing higher risk of Non-Hodgkin Lymphoma (NHL). Patients infected with HTLV may also present higher risk of caries, periodontal diseases and opportunistic infections, such as candidiasis. One of the largest predisposing factor is HTLV treatment, once the drugs may cause xerostomia and reduced salivary flow rates. HTLV infected patients are considered special needs patients due to possible neuropsychomotor alterations, which requires attention from the dentist. Also, the professional must be aware of oral manifestations to be able to properly instruct and treat a infected patient.

DETECTION OF HUMAN PEGIVIRUS (HPgV) IN HUMAN T LYMPHOTROPIC VIRUS POSITIVE PATIENTS IN THE CITY OF BELÉM, PARÁ.

de Lima, A.B.F.; de Sá, K.S.G.; de Sousa, J.L.S.; Torres, M.K.S.; Bezerra, D.A.M.; dos Santos, F.S.; Siqueira, J.M.; Resque, H.R.; Azevedo, V.N.; Soares, L.S.; Machado, L.F.A.

Universidade Federal do Pará.
biafgd@gmail.com

Human Pegivirus (HPgV) is a pan-lymphotropic RNA virus, and several studies correlate its co-infection with Human Immunodeficiency Virus (HIV) to positive effects for HIV-infected patients, as a lower HIV load. Nevertheless, there is a lack of data concerning to HPgV among people infected with other retroviruses as human T cell lymphotropic virus (HTLV), which is associated to disorders like adult T cell leukemia/lymphoma (ATL) and HTLV-1-associated myelopathy/tropical spastic paraparesis (PET/MAH). Therefore, this study aims to describe HPgV frequency among HTLV-positive individuals in Pará state, Brazil. Methods: To detect HPgV, a total of 74 blood samples collected between 2003 and 2016 from HTLV-positive individuals were submitted to nucleic acids extraction and quantitative polymerase chain reaction (qPCR). Quantitative and qualitative analysis based on clinical and epidemiological data from the patients enrolled were executed. Results and Conclusion: Overall, HPgV was found in 5,4% (4/74) of samples and, although no significant statistical differences have been noted regarding to age distribution, gender and clinical diagnostic in mono- and co-infected patients, to our knowledge, this is the first report of HPgV circulation in HTLV-positive individuals in Brazil. These findings encourage new researches aiming to enhance and establish the panorama of HPgV infections in HTLV-positive populations.

PHYLOGENETIC ANALYSIS OF HTLV-1 AND HTLV-2 TAX GENE DIVERSITY IN A COHORT FROM RIO DE JANEIRO, BRAZIL.

Gomes, Y.C.P.; Leite, A.C.C.B.; de Lima, M.A.S.D.; Araújo, A.C.Q.; Paulo, A.C.V.; Espindola, O.M.; da Silva, M.T.

Instituto Nacional de Infectologia Evandro Chagas - FIOCRUZ.
yago_gomes92@hotmail.com

HTLV-1 and HTLV-2 are epidemiologically relevant retroviruses in Brazil, and their genotyping is performed by analysis of LTR sequences. The HTLV-1 Cosmopolitan subtype, which is worldwide distributed, is subdivided into five groups: Transcontinental, Japanese, Caribbean/Africa, North Africa and black Peruvians. In turn, genetic analysis of HTLV-1 tax discriminates two subgroups: taxA and taxB, which are respectively associated to the Transcontinental and Japanese subtypes. Thus, we performed genetic analysis with fragments of 988bp and 645bp from tax of HTLV-1 (n=80) and HTLV-2 (n=12), respectively, in order to characterize polymorphisms in a cohort from Rio de Janeiro, Brazil. All HTLV-2 tax isolates were genotyped as 2c, which is predominant in Brazil. Likewise, all HTLV-1 isolates were characterized as taxA: 71 clustered as Latin American A subtype and 7 as Latin American B, which presents greater proximity to taxB. Indeed, 85% of HTLV-1 isolates displayed the five nucleotide substitutions associated to taxA (C7401T, T7914C, C7920T, C7982T and G8231A). Two silent mutations (T7974C and T8313C) were observed in 46.25% of HTLV-1 tax isolates and were restricted to the Latin American A cluster. Interestingly, subjects with these additional tax mutations displayed higher median HTLV-1 proviral load and therefore this association should be further investigated.

HUMANIZED NSG MICE AS A MODEL FOR HTLV-1 INFECTION: DIFFERENTIATION AND MODULATION OF T-CELLS DURING ESTABLISHMENT OF VIRAL PERSISTENCE.

Espindola, O.M.; Villaudy, J.; Rijnstra, E.S.; Frankin, E.; Weijer, K.; Velden, Y.V.D.; Berkhout, B.; Blom, B.

Instituto Nacional de Infectologia Evandro Chagas, Fundação.
otavio.espindola@ini.fiocruz.br

HTLV-1 is the etiological agent of adult T-cell leukemia (ATL), an aggressive malignancy of CD4⁺ T-cells with poor prognosis. Distinct animal models have been developed to study ATL, although with limitations. Here, we report an HTLV-1-infected humanized mouse model generated by intraperitoneal injection of human CD34⁺CD38⁻ hematopoietic stem cells into NSG mice. Upon infection, human T-cells rapidly increased in blood and the periphery, especially CD25⁺CD4⁺ T-cells. Proliferation of CD4⁺ T-cells in spleen and mesenteric lymph nodes (MLN) was determined by Ki67 expression, and correlated with HTLV-1 proviral load and CD25 expression. CD4⁺ and CD8⁺ T-cells predominantly displayed an effector memory phenotype (CD45RA⁻CCR7⁻) and expressed CXCR3 and CCR5 chemokine receptors, reflecting an HTLV-1-induced Th1 response. Activated CD8⁺ T-cells expressed both granzyme B and perforin, however, interferon-gamma response in these cells was limited, probably due to downregulation associated to elevated PD-1 expression and increased rates of FoxP3⁺CD4⁺ T-cells in MLN. In addition, splenomegaly, a common feature of ATL in humans, was present in 50% of mice after 60 days of infection. Thus, HTLV-1-infected humanized NSG mice reproduced many of the attributes of this infection as described in humans. Therefore, it may be useful in investigating initial events of ATL and to perform preclinical studies.

PHOTOTHERAPY IN LYMPHOPROLIFERATIVE AND INFLAMMATORY DISEASES ASSOCIATED WITH HTLV.

Lobato, B.A.L.; Carneiro, T.X.; Okajima, R.M.O.; Silva, C.A.M.; Abreu Junior, J.M.C.; Xavier, M.B.

Universidade do Estado do Pará.
brenasousa@gmail.com

Dermatological manifestations affect 5 to 10% of patients with HTLV-1, including asymptomatic ones. Phototherapy is a therapeutic modality with favorable response in lymphoproliferative and inflammatory skin disorders, due to its anti-inflammatory, antiproliferative and immunosuppressive properties. Objective: To evaluate the effectiveness of phototherapy in the treatment of lymphoproliferative and inflammatory diseases associated to HTLV. Methods: Twelve patients with inflammatory or lymphoproliferative dermatological diseases HTLV-positives (6) and HTLV-negatives (6) were selected through a convenience sample for treatment with narrow-band UVB phototherapy in the UEPA dermatology clinic. Patients underwent clinical evaluation and skin biopsy for histopathological examination, before and at the end of the 16th week of phototherapy. Results: The six patients HTLV-positives submitted to UVB-NB were serotype 1. The clinical evaluation showed improvement in the twelve patients studied, four presenting total regression of the lesions, seven with marked and one with moderate improvement after treatment. In histopathological examination, all five patients with lymphoproliferative disorders and five from the seven patients with inflammatory disorders presented regression in the majority of the evaluated parameters. Conclusion: Phototherapy was effective in the treatment of HTLV-associated lymphoproliferative and inflammatory skin diseases with improvement of skin lesions similar to those not infected by the virus.

SOME LABORATORY PARAMETERS AT DIFFERENT PERIODS IN VOLUNTEERS WITH HTLV-1 WITH MINOR NEUROLOGICAL SYMPTOMS.

Prates, G.S.; Assone, T.; Baldassin, M.P.M.; Kanashiro, T.M.; Paiva, A.M.; Haziot, M.E.; Smid, J.; de Oliveira, A.P.; Casseb, J

Institute of Tropical Medicine of São Paulo, São Paulo, SP, Braz.

Background: Despite classical HAM/TSP syndrome is the most neurological disturbance ascribed, some neurological disorders called “minor” are seen in “asymptomatic” HTLV-1 carriers. These disorders, including cognitive alterations, are usually not well characterized, and may constitute a true intermediate clinical syndrome between the asymptomatic and myelopathy state. Objective: Evaluate basal T-cell proliferation (LPA) in vitro and HTLV-1 proviral load (PVL) among HTLV-1-infected subjects who present minor neurological symptoms in three different points. Material and Methods: 235 confirmed HTLV-1 infection cases, without HAM/TSP diagnosis was clinically blinded assessed, in a regular follow-up at the HTLV outpatient clinic of the Institute of Infectious Diseases “Emilio Ribas”, Sao Paulo city, Brazil. These data were analyzed retrospectively. Samples were tested for PBMC spontaneous proliferation (LPA) and HTLV-1 proviral load (PVL). Results: From a total of 235 subjects with HTLV-1, 40 subjects presented minor neurological symptoms. The LPA and PVL of these 40 cases, showed similarly increase along time, without statistical significance. However, the number of clinical neurological symptoms was correlated to PVL ($p=0.003$). Conclusion: We observed a significant increase of PVL and 3 or more minor neurological symptoms.

ANTI-HTLV-I PREVALENCE IN LEPROSY PATIENTS IN THE PARAÍBA STATE, BRAZIL.

da Costa, J.E.F.; de Moraes, V.M.S.; Gonçalves, J.P.; Vasconcelos, A.O.; Coêlho, M.R.C.D.

Federal University of Pernambuco.
vivi.martha@hotmail.com

The immunological changes associated with leprosy/HTLV-I coinfection have a relevant clinical impact in patients, due to the interactions between HTLV-I and *Mycobacterium leprae* that can induce in the host an inflammatory response against mycobacterial antigens and consequently lead to the onset of a greater number of episodes reactions. The objective of this study was to estimate the prevalence of anti-HTLV in leprosy patients attended at the Sanitary Dermatology Outpatient Clinic in the Clementino Fraga Hospital Complex, in João Pessoa, Brazil, from 2015 to 2016. The commercial ELISA kit (HTLV I+II ELISA recombinant Wiener®) was used for anti-HTLV screening and the reagent samples were confirmed by the Western Blot kit (Fujirebio® INNO-LIA HTLV I/II Score). A total of 403 leprosy individuals were evaluated, being 53.59% (216/403) in the age group ≥ 45 years and 61.78% (249/403) males. The anti-HTLV prevalence by ELISA was 2.48% (10/403) and when confirmed by the Western blot technique, it was 0.99% (4/403). Considering that leprosy/HTLV coinfection has a relevant clinical impact that can trigger a greater number of reactional episodes, we emphasize the importance of early laboratory diagnosis of this infection, with the objective of providing information for better medical follow-up of the affected patients.

HTLV PREVALENCE AND RISK FACTORS IN PEOPLE LIVING WITH HIV/AIDS IN PERNAMBUCO AND PARAÍBA, BRAZIL.

de Souza, M.S.; Ribeiro, M.L.; de Moraes, V.M.S.; Gonçalves, J.P.; Coêlho, M.R.C.D.

Universidade Federal de Pernambuco.
rcoelholika@gmail.com

Studies suggest that coinfecting HIV/HTLV are more likely to develop myelopathies and neurological disease. In addition, coinfection may mask the diagnosis of human immunodeficiency syndrome, since TCD4⁺ counts could be increased in these individuals. The aimed of this study was to estimate the prevalence and risk factors associated with HIV/HTLV coinfection in Pernambuco and Paraíba, states of Northeast Brazil. The commercial ELISA kit (HTLV I+II ELISA recombinant Wiener®) was used for anti-HTLV screening and the reagent samples were confirmed by the Western Blot kit (Fujirebio® INNO-LIA HTLV I/II Score). The coinfection HIV/HTLV prevalence in patients followed up at the Clinical Hospital of the Federal University of Pernambuco, in the period from 2013 to 2016 was 1.5% (11/720) and ten patients as HTLV-1 and one as HTLV-2. In Paraíba, the coinfection HIV/HTLV prevalence was too 1.5% (6/401) in patients followed up at the Clementino Fraga Hospital, João Pessoa, from February to July 2015. No association was observed between the risk factors examined and HTLV/HIV coinfection in both studies. The low of coinfection HIV/HTLV prevalence and absence of association of risk factors differ from studies performed in other countries and other regions of Brazil, possibly due to the epidemiological, behavioral and cultural characteristics of the analyzed population.

STABILITY OF THE GLYCOPROTEIN 46 (gp46) GENE OF HTLV-1 IN AN ENDEMIC REGION OF THE BRAZILIAN AMAZON, AND THE PRESENCE OF AN IMPORTANT MUTATION (N93D) IN SYMPTOMATIC PATIENTS.

Viana, M.N.S.A.; Nobre, A.F.S.; Costa Junior, E.; Silva, I.C.; Pinheiro, B.T.; Pereira, C.C.C.; Covre, L.S.C.; de Almeida, D.S.; de Araújo, M.W.L.; Borges, M.S.; da Costa, C.A.; Ishikawa, E.A.Y.; Ferrari, S.F.; de Sousa, M.S.

Universidade Federal do Pará - Núcleo de Medicina Tropical.
maryvyana@hotmail.com

Background: The human T-lymphotropic virus type 1 (HTLV-1) affects 2–5 million people worldwide, and is associated with a number of degenerative and infectious diseases. The Envelope glycoproteins (gp) are highly conserved among the different HTLV-1 isolates, although nucleotide substitutions in the region that codifies these proteins may influence both the infectivity and the replication of the virus. The gp46 gene has functional domains which have been associated with the inhibition of the formation of the syncytium, cell-cell transmission, and the production of antibodies.

Objective: The present study investigated the genetic stability of the gp46 gene of HTLV-1 in an endemic region of Brazilian Amazonia.

Methods: Index case (IC - a sample of a given family group) carriers of HTLV-1 were investigated in the metropolitan region of Belém (Pará, Brazil) between January 2010 (registered retrospectively) and December 2015. The sequences that codify the gp46 were amplified by PCR, purified and sequenced (MF084788–MF084825). The gene was characterized using bioinformatics and Bayesian Inference.

Results: The 40 patients analyzed had a mean age of 45.2 years and 70% presented some type of symptom, with a predominance of pain and sensitivity, dysautonomia, and motor disorders. All patients presented the aA (Transcontinental Cosmopolitan) genotype, with an extremely low mutation rate, which is characteristic of the codifying region (aA – 1.83×10^{-4} mutations per site per year). The gp46 gene had a nucleotide diversity of between 0.00% and 2.0%. Amino acid mutations were present in 66.6% of the samples of individuals with signs/symptoms or diseases associated with HTLV-1 ($p = 0.0091$). Of the three most frequent mutations, the previously undescribed N93D mutant was invariably associated with symptomatic cases.

Conclusions: The aA HTLV-1 subtype is predominant in the metropolitan region of Belém and presented a high degree of genetic stability in the codifying region. The rare N93D amino acid mutation may be associated with the clinical manifestations of this viral infection.

THE CO-INFECTION BETWEEN HIV I / HTLV I AND ITS CLINICAL IMPLICATIONS.

Vieira, E.S.; Melo, B.L.; de Carvalho, G.C.P.; dos Passos, J.L.; Sacramento, L.S.; Lessa, D.S.

Escola Superior da Amazônia – ESAMAZ.
biomedicodiegolessa@gmail.com

Introduction: The coinfection between Human Immunodeficiency Virus 1 (HIV 1) and Human T-Cell Lymphotropic Virus (HTLVI) can occur frequently, which is because they share the same infection routes, as well as reaching the same types of cells, that is, the T lymphocytes. Aim: The study aims to make a bibliographic survey to analyze the implications and the aggravation caused by the coinfection of HTLVI/HIV1 viruses. Methodology: Study of bibliographic review in recognized databases in the academic- scientific environment, such as: Scielo, Pubmed, Science direct, Scopus. Results: The most frequent transmission routes were needle sharing between injecting drug users and sexual intercourse, mainly in males, aged from 15 to 84 years, patients had a significant increase in the number of CD4 + T cells and reported they have been affected by opportunistic infections, in addition to the development of HAM/TSP. Conclusion: The increase in CD4 + T cells does not represent an advantage over the immune response, and may induce a medical error at the right time to initiate antiretroviral therapy and/or prophylaxis against opportunistic infections, which can lead patients to a more rapid progression to AIDS .

ANALYSIS OF STING GENE EXPRESSION IN PATIENTS WITH HTLV-1 WITH HAM/TSP DIAGNOSIS.

Lima, S.N.; Queiroz, M.A.F.; Monteiro, J.C.; Feitosa, R.N.M.; Ishak, R.; Vallinoto, A.C.R.; da Silva, A.N.M.R.

Federal University of Pará-UFPA, Institute of Biological Science
samaranascimento_lima@hotmail.com

The stimulator of interferon genes (STING) is an important signaling molecule involved in the innate immune response and its expression profile may play a role for the progression of HTLV-1 associated myelopathy/tropical spastic paraparesis (HAM/TSP) disease. This study aimed to analyze the gene expression levels of STING, among HTLV-1 carriers and its association with the progression for HAM/TSP. To evaluate the expression of STING, the work was conducted in HTLV-1 patients with HAM/TSP (n=10), asymptomatic individuals (n=10) and seronegative controls (n=10). Quantitative analysis of the mRNA expression levels were performed by Real-Time PCR, using the TaqMan™ technology. The relative quantification (RQ) of the gene expression of the target genes (STING and GAPDH) was determined by the comparative CT method ($\Delta\Delta CT$). Statistical analyzes were performed using the non-parametric Mann-Whitney test ($p < 0.05$). The results demonstrated that there was no statistically significant difference ($p = 0.3760$) in the STING expression levels between HAM/TSP and asymptomatic patients. However, when comparing the levels of gene expression among HTLV-1 carriers with the control subjects, a statistically significant difference was observed ($p = 0.0028$). In conclusion, there was no evidence that STING expression contributes to HTLV-1 carriers evolving for HAM/TSP.

DRUG REPURPOSING AS NEW STRATEGY FOR TREATMENT OF HTLV-1 INFECTION AND ASSOCIATED DISEASES.

dos Santos, D.F.; de Pilger, D.R.B.; Khouri, R.; Casseb, J.; Freitas-Junior, L.H.; Kashima, S.

Faculdade de Medicina de Ribeirão Preto
daiane_biomed@yahoo.com.br

There is no cure and no vaccine for human T cell lymphotropic virus type 1 (HTLV-1) infection. Therapeutic approaches for the main associated diseases (HTLV-1 associated myelopathy/tropical spastic paraparesis-HAM/TSP, and adult T cell leukemia/lymphoma-ATL) have variable effectiveness. Thus, identifying and developing new uses for existing drugs is considered a suitable strategy for antiviral therapy. Aim. To screen 707 FDA-approved compounds from the NIH library using a resazurin reduction assay for identification of cell proliferation inhibitors in HTLV-1-infected cell line (MT-2). Methods. MT-2 cells were plated with 707 compounds (final concentration: 5 μ M) and resazurin reduction method was adopted. Hits (compounds with activity \geq 50%) were selected for dose-response curve (DRC) assays. Results. From 707 compounds, 34 hits were identified in primary screening. Z-factor for all plates were satisfactory (\geq 0.5) and Pearson's correlation coefficient between two assays were $r = 0.85$. Next, five hits were confirmed as drug candidates in DRC assays and EC₅₀ of each one was determined: disulfiram (0.26 μ M), cytarabine (0.15 μ M), chlorambucil (3.0 μ M), cladribine (0.12 μ M) and galantamine hydrobromide (28 μ M). Conclusion. Five FDA-approved drugs were able to decrease MT-2 proliferation. Thus, drug repurposing can be applied to investigate new strategies for HTLV-1 infection treatment.

TREX1 531C/T POLYMORPHISM IN HTLV-1 INFECTION.

Silva, D.C.; Amoras, E.S.G.; Moura, T.C.F.; Gomes, S.T.M.; Lopes, F.T.; Ishak, R.; Vallinoto, A.C.R.; Queiroz, M.A.F.

Universidade Federal do Pará
denisdecastrosilva@gmail.com

(three-prime repair exonuclease 1) is a host factor that facilitates retroviral infection acting as a negative regulator of the interferon response to DNA derived from both endogenous retro-elements and exogenous retroviruses. Mutations in the enzyme genes can alter DNA repairs, leading to DNA accumulation derived from retroviruses, which will induce interferon production and an immune-mediated inflammatory response, promoting autoimmunity. HTLV-1 infection is also known to promote tolerance loss and autoimmunity. The present work investigated TREX1 531C/T polymorphism influence on the susceptibility and disease development related to HTLV-1 infection. The study included 152 infected persons (31 clinically diagnosed as HAM/TSP, 2 with a diagnosis of probable HAM/TSP, 19 with rheumatologic manifestations, 2 with dermatitis, 5 with more than one clinical diagnosis, and 91 asymptomatic carriers) and a control group, consisting of 100 individuals with a risk exposure behavior and laboratory negative diagnosis for HTLV-1/2, HIV-1, HBV and HCV. Genotyping of TREX1 531C/T and HTLV-1 proviral load were performed by real time PCR assay. TREX1 531C/T polymorphism analysis showed that the wild CC genotype was the most frequent in all groups investigated, but no genotypes or alleles were associated with susceptibility to HTLV-1 infection. The polymorphism was not associated with symptoms related to HTLV-1 infection, but asymptomatic carriers showed higher frequency of CT genotype, than patients with HAM/TSP ($p=0.0305$). HTLV-1 proviral load were higher among individuals with CT/TT genotypes, regardless of the presence of symptoms, but there was no statistical significance. The results suggest that TREX1 531C/T polymorphism is not associated with susceptibility to HTLV-1 infection nor with the infection-related disease development. However, the polymorphic genotypes seem to favor the infection, since individuals with these genotypes presented higher HTLV-1 proviral load. Additional studies will be conducted to investigate the polymorphism influence on production of autoantibodies and type I IFN.

EFFECT OF A PROTOCOL FOR MUSCLE STRENGTH OF LOWER LIMBS ON THE MOBILITY OF PATIENTS WITH TROPICAL SPASTIC PARAPARESIS - TSP/HAM.

Silva, D.C.; da Cunha, B.C.S.; de Oliveira Fampa, S.G.C.O.; de Andrade, A.A.S.; Pinto, D.S.

Universidade Federal do Pará – UFPA
dihego30@hotmail.com

Introduction: Human T-cell lymphotropic virus (HTLV-1) is the etiologic agent of several diseases such as HTLV-1 associated with Tropical Spastic Paraparesis. In individuals who develop TSP/HAM, due to the involvement of muscle groups of the lower limbs and pelvic girdle, the main symptoms are gait disturbances, with a tendency to risk of falls, in addition to muscle weakness. The objective of the research to verify the effect of muscle strengthening program on the mobility of patients with TSP/HAM. Methodology: The protocol described in this study had as a locus the Laboratory of Studies in Functional Rehabilitation (LAERF). Opinion Ethics Committee: 063-2011-CEP / NMT / UFPA. After initial evaluation through the Medical Reserach Council Scale and the Time Up And Go Test, patients underwent a 10-session twice weekly program of one hour (hip flexion, knee flexion and extension, initiating without load and progressing with load of up to 5 kg). In addition, all signed the Term of Free and Informed Consent - TCLE. Results: The initial evaluation of muscle strength showed a slight decrease in strength in LMW for the muscular groups evaluated (iris, hamstrings and quadriceps) with grade 4 in the RME in the 5 patients, in both MID and MIE. In the mobility test three patients presented total time in the TUG between 20 and 30 seconds, one presented total time of 12 seconds and one remained within the normal range with 8 seconds of duration. In the final evaluation of muscle strength, the three muscle groups evaluated had a grade 5 in the RMSE in both MID and MIE, and the time spent on the mobility test after the 10 sessions decreased in all 5 patients, and the three who started with time between 20 and 30 seconds ended with results between 10 and 20 seconds, the patient who started with 12 seconds, finished with time less than 10 seconds and what was with time less than 10 seconds remained with result within the normality. Conclusion: The proposed MMII muscle strengthening protocol obtained satisfactory results in the mobility of patients with TSP/HAM.

EVALUATION OF CHEMILUMINESCENCE TEST RESULTS IN GENOTYPED SAMPLES FOR HTLV-I AND HTLV-II ON INAPT BLOOD DONORS OF A BRAZILIAN BLOOD BANK.

Macêdo, J.M.O.; Rodrigues, S.V.; Barroso, C.F.; Paula, L.C.C.; Monteiro, L.A.; do Nascimento, L.N.S.; Barile, K.A.S.; Amaral, C.E.M.

Universidade do Estado do Pará (UEPA), Belém, Brasil.
joamaarcos@gmail.com

Brazil is among the countries with the highest absolute number of HTLV, being a risk of transmission of HTLV through blood transfusions. Thus, screening for HTLV has been done in Brazil since 1993. This study aimed to conduct a comparative analysis between the tests used to investigate HTLV infection and determine possible correlations between these tests. Donors' samples treated in Hemopa from 2014 to 2017 presenting results above 0.8 on chemiluminescence test for HTLV I/II were analyzed. Specimens with S/CO < 0.8 were considered nonreactive and S/CO ≥ 0.8, reactive. In the data analysis, average values, standard deviation and minimum and maximum values were calculated. Comparison of averages was performed by Student's t-Test. 610 samples presented reactive in serological screening. 390 with S/CO greater than 1.2, 220 with values between 0.8 and 1.2 (all of these, PCR undetectable). Of the 390 samples, 26.4% presented HTLV-I, 6.6% HTLV-II, and in 67% PCR undetectable. Values of the samples on chemiluminescent test were evaluated: HTLV-I samples ranged from 18.83 to 210.95, average: 106.16 ± 49.76, HTLV-II ranged from 20.94 to 164.80, average: 95.24 ± 31. There was no significant difference between the averages. Approximately 70% of samples were possibly false-positive on chemiluminescent test.

EVIDENCE OF FALSE-POSITIVE RESULTS IN THE SCREENING OF ANTI-HTLV-1/2 ANTIBODIES IN HIV-1 INFECTED PATIENTS.

Lima, I.T.; Mendes, W.R.B.; Macêdo, O.; de Moura, A.; dos Reis, R.M.; de Freitas, R.C.A.; Freitas, F.B.

Instituto Evandro Chagas /SVS/MS
igortenorio003@gmail.com

Introduction and Objective: The HTLV-1/2 having the same route of transmission of HIV-1, this fact allows for a possible co-infection needing to be investigated, whereas in people living with HIV/AIDS (PLWHA), the prevalence of HTLV is greater, as well as risk of developing diseases associated with this virus. The objective of the study was to investigate the prevalence of HTLV-1/2 infection in PLWHA. **Methods:** 89 serum samples from individuals enrolled at the Evandro Chagas Institute, Brazilian Ministry of Health, diagnosed for HIV-1, were investigated during the year of 2017. We used an ELISA-type immunoassay, third generation (DIA-PRO, Italy), for the detection of total anti-HTLV-1/2 antibodies. To confirm HTLV-1/2 infection, real-time PCR methodology (qPCR) was used. **Results:** All the controls of the test were valid and in accordance with the value of the cut-off (0.350), 44 (49%) samples were positive (OD > 1.1), 35 (39%) negative (< 0.9) and 10 (11%) undetermined (0.9-1.1). Among the positive samples, the ones with the highest optical density were selected, totaling 15 samples (OD: 1,147-2,997) for confirmation by the q-PCR. Positive and negative controls were used and endogenous control of reaction (human beta globin) was detected in all samples, but all samples were negative for HTLV-1/2 proviral DNA. **Conclusions:** All the samples tested showed an undetectable result in the qPCR, evidencing a great disagreement among the methodologies. The low specificity of the screening assays in the detection of anti-HTLV antibodies could favor the emergence of cross-reactions with other infectious agents, which highlights the need for the creation and standardization of more precise protocols in the laboratory diagnosis of this infection, especially in specific populations such as PLWHA.

FORCE PLATFORM INDICATES BALANCE IMPAIRMENTS IN HTLV-1 INFECTION.

Vasconcelos, B.H.B.; Callegari, B.; Barroso, T.G.C.P.; Silva, A.A.C.; Saunier, G.; Sousa, R.C.M.; Xavier, M.B.; Souza, G.S.

Universidade Federal do Pará.
beatrizhelenaglobo.com

HTLV-1 is a retrovirus of the Retroviridae family that infects CD4 T lymphocytes and stimulates their proliferation. A severe consequence of this infection can be the HTLV-1 associated myelopathy /tropical spastic paraparesis (HAM/TSP), which is associated to a progressive demyelinating disease of upper motor neurons. The HAM/TSP conditions frequently presents neurological complaints as gait impairment, sphincter disturbances and several sensory losses. The aim was quantified the balance control in HTLV-1 patients, with and without HAM/TSP, using a force platform and comparing them to healthy subjects. Methods: We studied 19 HTLV-1 patients, 18 HAM/TSP patients, and 34 healthy subjects. We compared the individual data from the HTLV-1 and HAM/TSP subjects to the normative limits of the control group for the different control balance parameters, with eyes open and closed. Results: We found that 16 HAM/TSP patients and 4 HTLV-1 infected patients had balance impairments based on the center of pressure deviations. The group comparison showed that HAM/TSP patient group had worse control balance than HTLV-1 infected patient and control groups in test conditions. Conclusion: These results imply that posturographic parameters can be sensible to identify subtle changes in the balance of HTLV-1 patients and to monitor the neurological damage of them.

HAM/TSP INCIDENCE IN 20 YEARS OF FOLLOW-UP IN A PROSPECTIVE COHORT STUDY.

Romanelli, L.C.F.; Ribeiro, M.A.; Ferreira, A.S.D.; Gonçalves, D.U.; Starling, A.L.B.; Martins, M.L.; Proietti, A.B.F.

Fundação Hemominas, Belo Horizonte, Brazil

Background: The incidence of HTLV-1-associated myelopathy (HAM) is variable according to literature, which may be due to the differences in age, gender proportion, the follow-up time of the studies as well as to the characteristic differences of each population. **Objective:** This study aimed to evaluate the incidence of HAM in individuals followed-up for 20 years by the GIPH Cohort. **Methods:** GIPH study is an open cohort that started in 1997 the follow-up of HTLV-1/2 infected carriers, composed mostly of deferred blood donors and their relatives. GIPH cohort participants were called every two years for epidemiological, clinical and laboratory evaluation. In 2007 neurological evaluation was introduced with the same periodicity. For the analysis of HAM incidence, we considered all participants who underwent neurological evaluations from 2007 to 2017 (n=334). We excluded 58 individuals who had less than 6 months of follow-up by GIPH, 27 who were enrolled to the cohort with possible or defined HAM and 7 individuals who presented other neurologic/infectious diseases that compromised the differential diagnosis of HAM. **Results:** The mean age of total population (n=242) was 49 years with a predominance of female gender (n=148, 61%). The mean follow-up time was 10 years (7 months-20 years) and the follow-up time sum of the total population was 2,492 years. Considering the included 242 HTLV-1 asymptomatic carriers, 12 evolved to HAM during the follow-up. The HAM incidence rate was 4.81 cases/1000 HTLV-1 infected/year. In the HAM incident group 75% (n=9) were female, and the mean age was 46 years. **Conclusion:** Diseases of low prevalence and slow progression, such as HAM, require cohort studies with long follow-up of large population to obtain a reliable incidence rate. On the other hand, long-term cohort studies are difficult because of low adherence and confusion factors such as emergence of diseases related to aging. In spite of these difficulties, the HAM incidence rate calculated after 20 years of follow-up was very close to that observed previously in our cohort after 10 year of follow-up, that was 5.3 cases/1000 HTLV-1 infected/year. The present study showed that a HAM incident rate around 5 cases/1000 individuals/year is expected for the Brazilian HTLV-1-infected population.

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HTLV-1 SPECIFIC IMMUNE RESPONSE IN HAM/TSP PATIENTS AND ITS VARIATION DURING TREATMENT WITH METHYLPREDNISOLONE AND METHOTREXATE.

Rosadas, C.; Rowan, A.; Taylor, G.

Imperial College London, Estácio.
carolrosadas@gmail.com

HTLV-1 causes an immune imbalance which plays a central role in the pathogenesis of HAM/TSP. The knowledge about the impact of treatment in HTLV-1 immune response is poor. The objective was to evaluate the specific immune response to Tax and HBZ in HAM/TSP patients and its variation according to treatment. We studied 6 HAM/TSP patients treated with methylprednisolone (MP) followed by methotrexate (MTX). Patients underwent clinical evaluation and samples were collected at multiple time points. Six asymptomatic carriers (AC) were also evaluated once. PBMCs were cultured for 6h with medium only, peptides from Tax and HBZ, or PMA/Ionomycin. Cells were stained with viability stain, anti-CD3-FITC, CD4-APC-Cy7, CD8-AlexaFluor700, TNF- α -BV605, IFN- γ -PE-Cy7, MIP-1 β -APC and IL-2-PE. The frequency of Tax-specific T lymphocytes was greater than HBZ-specific lymphocytes, and the frequency of cytokine producing CD8⁺ cells was greater than CD4⁺. IL-2+CD4⁺ cells were detected only in one patient during treatment with MTX. Patients who improved showed an increase in Tax-specific-CD4⁺MIP-1 β ⁺ cells, while those who deteriorated showed a decrease. Untreated HAM/TSP patients had a low frequency of Tax-specific-CD4⁺MIP-1 β ⁺ cells when compared with ACs. We conclude that HAM/TSP patients can respond to HTLV-1 proteins despite immunosuppressive treatment, and that Tax-specific-CD4⁺MIP-1 β ⁺ cells may be associated with protection.

PROGRESSIVE NEUROLOGICAL DAMAGE IN HTLV-1 INFECTION ANALYSED BY BAREFOOT PLANTAR PRESSURE.

Vasconcelos, B.H.B.; Souza, G.S.; Barroso, T.G.C.P.; Silveira, L.C.C.; Sousa, R.C.M.; Callegari, B.; Xavier, M.B.

Universidade Federal do Pará.
beatrizhelenaglobo.com

HTLV-1 is a retrovirus associated with neurological alterations in patients who developed HTLV-1 associated myelopathy / tropical spastic paraparesis (HAM/TSP). Frequent neurological complains comprise foot numbness and leg weakness. The purpose of this study was to compare the pressure distribution in different areas of the foot plantar region in three groups of subjects: HTLV-1 patients with HAM/TSP, asymptomatic HTLV-1 patients, and healthy controls. Methods: We studied 18 HTLV-1 patients with HAM/TSP, 18 asymptomatic HTLV-1 patients, and 17 control subjects. Screening evaluation comprised clinical interview, reflexes examination, feet sensitivity evaluation, and risk of fall. Pressure distribution in the foot plantar region was measured with baropodometry, with patient eyes open and closed. Results: Prevalence of neurological disturbance – altered reflexes, feet sensitivity alteration, and risk of fall – was higher in HAM/TSP patients than HTLV-1 asymptomatic patients. The medium and maximum pressure values were higher in the forefoot than in the midfoot and hindfoot of both groups. In addition, the hindfoot pressure was lower in the HAM/TSP patients than control group. Conclusion: There is a progression of baropodometry findings from controls to HTLV-1 asymptomatic patients to HTLV-1 HAM/TSP patients. Baropodometry is a valuable exam to establish the neurological damage in patients with HTLV-1.

PROVIRAL LOAD DOES NOT INFLUENCE CYTOKINE PRODUCTION IN ASYMPTOMATIC HTLV-1 CARRIERS.

Moura, T.C.F.; Amoras, E.S.G.; Santana, B.B.; Azevedo, V.N.; Feitosa, R.N.M.; Ishak, R.; Vallinoto, A.C.R.; Queiroz, M.A.F.

Universidade Federal do Pará, Instituto de Ciências Biológicas.
tuanecfmoura@gmail.com

HTLV-1 infection is the etiology of TSP/MAH, a disease with a high level of proviral load and an intense inflammatory process. However, although asymptomatic carriers may present increased levels of proviral load, it is important to evaluate immuno-inflammatory markers which can lead to the emergence of symptoms associated with the infection. The present study investigated TNF- α , IFN-gamma, IL-6, IL-8 and IL-10 production among 71 HTLV-1 infected persons (20 clinically diagnosed as TSP/HAM and 51 asymptomatic carriers). HTLV-1 proviral load was determined using a real time PCR assay and cytokines plasma levels were measured using an enzyme immuno assay (ELISA). Proviral load, TNF- α and IL-10 levels were significantly higher among those with HAM/TSP compared with asymptomatic individuals ($p=0.0069$, $p=0.0023$, $p=0.0317$, respectively). IFN-gamma levels were also higher among diseased persons, but showed no statistical significance. In contrast, IL-6 and IL-8 levels were higher in the asymptomatic group, although proviral load levels variation did not significantly influence the production of cytokines. The present work emphasizes that TSP/HAM patients present detectable proviral load and high levels of proinflammatory cytokines (TNF- α and IFN-gamma) and IL-10, which is possibly produced as an attempt to control the inflammatory process. The low levels of IL-6 and IL-8 among the patients may be a consequence of the advanced stage of disease, in which the innate immunity mechanism action is less intense. The same is not true when dealing with asymptomatic individuals as high proviral load levels do not influence the production of cytokines. Thus, proviral load quantification by itself may not be a reliable tool to predict the progression of HTLV-1 infection to disease development. Other important variables are possible modulators of the inflammatory activity which maintains homeostasis among HTLV-1 carriers with high proviral load.

SAMHD1 RS6029941 (A/G) POLYMORPHISM INFLUENCES THE PROVIRAL LOAD LEVELS AND THE RISK FOR HAM/TSP.

Amoras, E.S.G.; Queiroz, M.A.F.; Moura, T.C.F.; Ishak, R.; Vallinoto, A.C.R.

Universidade Federal do Pará, ICB, Laboratório de Virologia.
ednelza@hotmail.com

SAMHD1, a host dNTPase acts as a retroviral restriction factor degrading the nucleotide pool available to the initial reverse transcriptase of HTLV-1 among other retroviruses. Polymorphisms in SAMDH1 may alter enzyme expression and influence the course of virus infection. The present study investigated the influence of polymorphisms on the susceptibility to HTLV-1 infection and progression to disease and involved 108 HTLV-1 infected individuals (23 HAM/TSP, 18 rheumatologic manifestations, 2 dermatitis, 1 uveitis, 3 with more than one clinical diagnosis and 61 asymptomatic) and a control group of 100 individuals with risky exposure behavior and negative diagnosis for HTLV-1, HIV-1 and viral hepatitis. Genotyping of rs6029941 (G/A) and HTLV-1 proviral load (PVL) were performed by a real time PCR assay. The wild AG genotype of SAMHD1 rs6029941 was the most frequent among HTLV-1 infected and control groups, but no genotype or allele was associated with susceptibility to HTLV-1 infection. The AG genotype was the most frequent among HTLV-1 infected asymptomatic and symptomatic groups, but there was no association with the presence of disease. A high frequency of genotype AA and allele A was present among HAM/TSP patients ($p=0.0327$ and $p=0.0019$, respectively) and allele A was associated with an increased chance of clinical progression to HAM/TSP (OR= 2.7, $p=0.0019$). PVL levels were significantly higher among infected individuals with GG genotype ($p=0.0326$, $p=0.0382$, respectively), regardless of the presence of symptoms. This suggests that SAMHD1 polymorphism permits virus escape to the restriction factor leading to increased HTLV-1 replication and the presence of allele A favors viral replication control leading to lower levels of PVL. The intense immunological response of several system components, as well as SAMHD1, seems to induce an exacerbated inflammatory process and the emergence of disease, particularly HAM/TSP, HTLV-1 infected persons carrying allele A presented almost three times more chance to develop HAM/TSP.

SIDE EFFECTS IN ORAL CAVITY OF PATIENTS SUBMITTED TO THERAPY AGAINST HUMAN T CELL LYMPHOTROPIC VIRUS.

Oliveira, J.A.A.; Gatinho, J.J.M.; Leitão, A.L.A.P.; de Sousa, T.C.V.; Nagase, A.A.; Gatinho, M.M.M.

Universidade Federal do Pará.
jessicalineao@outlook.com

The treatment applied to control the side effects of HTLV reverberates on several parts of the body, including the oral cavity. The objective of the study was to review literary findings of the main oral sequels induced by the anti-retroviral treatment. The research markers employed were “HTLV”, “Human T-cell lymphotropic virus” and “oral cavity” in English and Portuguese in the Google scholar, Scielo, PubMed and Lilacs databases. The standard applied was the scientific researches produced in the last ten years. Damages to the oral cavity caused by drug therapy is primarily related a variance in the quality of saliva and / or the salivary flow. The main drug classes used are hormones, antidepressants and anticonvulsants, antibiotics and antiretrovirals, which have as their most frequent side effects herpetic lesions in the mouth, xerostomy, mouth ulceration, gingival hyperplasia and altered taste, respectively, which if untreated, can progress to more severe pathologies or act as a gateway to opportunistic infections. In view of the oral sequels described in this study, it is possible to comprehend that there is a need for a multidisciplinary team working in for the recovery of patients infected by HTLV, where the dentist is a key element.

COMPARATIVE STUDY BETWEEN THE DIAGNOSIS FOR TECHNICIANS SOROLOGIES AND OF THE QPCR FOR A DETECTION OF HTLV - I IN THE DONORS' SELECTION IN THE FOUNDATION HEMOPA.

do Nascimento, L.N.S.; Rodrigues, S.V.; Macêdo, J.M.O.; Monteiro, L.A.; Barroso, C.F.; Barile, K.A.S.; Amaral, C.E.M.

University of the State of Pará (UEPA), Belém, Brasil.
laianenazare14@gmail.com

HTLV doesn't have cure, it is asymptomatic and his diagnosis with difficulty is done before the appearance of the diseases to which the virus is associated. The risk of transmission of HTLV through blood transfusions motivated at several countries the accomplishment of the donors' of blood selection for this virus. The results of the tests were analysed sorologies and molecular of the samples of donors attended in the Foundation Hemopa of August of 2014 to December of 2017, in the study there were included samples originating from candidates for the donation of blood, which selection serologic presented positive result (S/CO>, 1,2) for HTLV-1 totalizing 298 samples. The selection serologic and molecular in the Foundation Hemopa it is carried out by the method of chemilumination, ARCHITECH rHTLV1/2, and the tests qPCR TaqMan. Of the samples studied with serology it makes (212/298) positive they were qPCR undetectable, of this 188 had relation S/CO between 1,2-11. Among the samples detected in the qPCR (86) 48 they were in the belt of S/CO 12-110 and 37 in the belt of 111-210. In this study, it was noticed that there can be an association between determined results serologic and presence of DNA proviral.

CORRELATIONAL STUDY BETWEEN PAIN INTENSITY, MOBILITY AND FALL RISK IN PATIENTS WITH HTLV-1-ASSOCIATED MYELOPATHY/TROPICAL SPASTIC PARAPARESIS.

da Cunha, B.C.S.; Balieiro, J.J.; da Silva, D.C.; da Costa, S.G.C.O.V.; de Souza, B.R.; Fonseca, Y.M.; de Andrade, A.A.S.; Pinto, D.S.

Universidade Federal do Pará (UFPA)
biancafisioufpa@gmail.com

Introduction: HAM/TSP (HTLV-1- Associated Mielopathy/ Tropical Spastic Paraparesis) is a spinal cord inflammation, seen in some people infected with the Human T - Lymphotropic Virus Type 1. Patients with HAM/TSP have numerous sensory symptoms, which includes low back pain, been mentioned as frequent, it's present in most patients represents an incapacity symptom. Altered body balance, other characteristic of these patients, can affect functional mobility, predisposing the patient to an increased risk of falls. In this way, these study is developed with the objective of correlate low back pain, mobility and fall risk. **Methods:** The study is characterized by being quantitative, descriptive, of the transverse tipe. Developed in 10 patients carrers HAM/TSP. The intensity of low back pain was measured by Visual Analog Scale, and the mobility and fall risk was measured by Time Get Up and Go test (TUG). **Results:** In the majority of HAM/TSP patients studied (90%), pain intensity was moderate, by the evaluation of Visual Analog Scale, while the mobility and fall risk were high in 60% of these patients ($p=0,0283^*$). **Conclusion:** There was a statistically significant correlation between pain intensity and decreased mobility, as well as an increased risk of falls in patients carriers HAM/TSP.

EFFECTS OF PILATES EXERCISE ON THE CLINICAL AND IMMUNOLOGICAL PROFILES OF PATIENTS WITH HUMAN T-CELL LYMPHOTROPIC VIRUS TYPE 1 (HTLV-1)-ASSOCIATED MYELOPATHY/TROPICAL SPASTIC PARAPARESIS.

Klautau, A.V.; Pinto, D.S.; Sousa, R.C.M.; Queiroz, M.A.F.; Santana, B.B.; da Silva, A.N.R.; Cayres-Vallinoto, I.M.V.; Ishak, R.; Vallinoto, A.C.R.

Universidade Federal do Pará, ICB, Laboratório de Virologia.
altairklautau@yahoo.com.br

Human T-cell lymphotropic virus type 1 (HTLV-1) is associated with human diseases such as Sjögren's syndrome, arthropathies, uveitis, dermatitis, adult T-cell leukemia/lymphoma (ATLL) and HTLV-1-associated myelopathy/tropical spastic paraparesis (HAM/TSP), a chronic inflammatory neurodegenerative disease. The aim of this study was to evaluate the effects of serial Pilates exercises on the clinical and immunological profiles of patients with HAM/TSP. Eight patients with ages ranging from 39 to 70 years old (2 males and 6 females), 2 wheelchair users and 6 with compromised gait, were evaluated. Data were collected at 3 time points (1st Ev – beginning of the study, 2nd Ev - after 20 Pilates sessions and 3rd Ev - after 10 weeks without Pilates) and consisted of evaluations of the pain level (Visual Analogue Scale), spasticity (Modified Ashworth Scale), motor strength (Motor Force Scale), balance (Trunk Impairment Scale, Tinetti), mobility (Timed Up and Go), functional capacity (FIM), quality of life (SF-36 questionnaire) and quantification of serum cytokine levels (IFN- γ , IL-10 and IL-9). After the Pilates sessions, significant improvements in pain level, static and dynamic balance, trunk control, mobility and quality of life were observed, with simultaneous and significant reductions in the serum levels of the cytokines IFN- γ and IL-10. However, after 10 weeks without Pilates, there were significant changes in terms of increasing pain and regression of mobility, with no changes in strength, spasticity, functional capacity and the other components of the SF-36 in any of the periods of the study. Thus, this study suggests that Pilates may help attenuate the clinical picture of HAM/TSP, possibly through the reduction of tissue inflammation. The results show the importance of introducing this type of treatment into physical therapy programs for patients with HAM/TSP to promote greater functional independence and increased quality of life.

EVALUATION OF THE LIMITATION OF ACTIVITY, RISK CONSCIOUSNESS, SOCIAL PARTICIPATION, QUALITY OF LIFE AND PAIN OF PERSONS WITH HTLV-1 CARRIERS OR NOT PET / MAH.

Aben-Athar, C.Y.U.P.; Santana, B.B.; de Sousa, M.S.; da Costa, C.A.; Pinto, D.S.; Vallinoto, A.C.R.

Laboratorio de Virologia, Instituto de Ciências Biológicas,
abenathar_cintia@hotmail.com

HTLV-1-associated myelopathy/tropical spastic paraparesis (HAM/TSP) has consequences in the quality of life of the patients. Objective: We aimed to evaluate the limitation of activity, risk awareness, social participation, quality of life and pain among 55 HTLV-1 infected individuals. Methodology: It was an observational, descriptive, analytical, cross-sectional study with quantitative approach. The screening of Activity Limitation and Safety Awareness (SALSA), the Participation Scale, the quality-of-life questionnaire (QOL) SF-36 and the Brief Pain Inventory (BPI) were used. Results: Asymptomatic patients had no activity limitation (64.71%) and symptomatic patients presented mild limitation (57.14%). None of the groups had a good risk awareness. There was no restriction on social participation in both asymptomatic (97.06%) and symptomatic (52.38%). The two groups complained of pain, being more frequent in the lumbar spine in the asymptomatic group, and in the knees among symptomatic subjects. The pain was more intense in the symptomatic patients, with interference in all aspects of SF-36. It was observed a higher quality of life in the asymptomatic when compared to the symptomatic. Conclusion: It should be emphasized that these aspects should be investigated more closely to improve assistance and help in the construction of public policies.

EVALUATION OF THE RESULTS OBTAINED IN THE HTLV-1/2 CONFIRMATORY TEST IN BLOOD DONATION CANDIDATES ATTENDED AT THE HEMOPA FOUNDATION - PARÁ.

Barroso, C.F.; Rodrigues, S.V.; Macêdo, J.M.O.; Lobato, A.M.V.; Monteiro, L.A.; do Nascimento, L.N.S.; Barile, K.A.S.; Amaral, C.E.M.

Universidade do Estado do Pará (UEPA), Belém, Brasil
camilabarroso17@gmail.com

The Human T-Cell Lymphotropic Virus (HTLV) belongs to the family Retroviridae, presents four types: HTLV-1, HTLV-2, HTLV-3 and HTLV-4. According to estimates, Brazil is among the countries with the highest absolute number of HTLV-infected individuals worldwide. The objective of this study was to evaluate the results of serological and molecular screening for HTLV 1/2 in blood donors at the HEMOPA Foundation. Samples reactive in the Chemiluminescence-HTLV-1/2 test, from 08/2014 to 12/2017, were analyzed and submitted to qPCR as a confirmatory test. Average and median, coefficient of variation, standard deviation and minimum and maximum values of cycles threshold (ct) of the samples were evaluated. In the study period, 610 samples presented reactive results in anti-HTLV 1/2 serological screening, of which 129 (21%) had detectable proviral DNA in qPCR: 103 (79.8%) HTLV-I and 26 (20.2%) HTLV-II. As for the ct of the HTLV-1 and HTLV-2 samples: HTLV-1 ct ranged from 21.95 to 41.55, with average of 29.92 ± 4.77 , median of 29,35 and CV = 15.93%. HTLV-2 ct ranged from 33.33 to 44.04 with average of 32.67 ± 6.18 , median of 32,67 and CV = 18.62%. Based on results, the HTLV-1 presented higher viral load at the time of detection when compared to HTLV-2.

FREQUENCY OF HTLV INFECTION IN A BLOOD BANK OF THE BRAZILIAN AMAZON REGION, FROM 2010 TO 2017.

Costa, L.A.; Lima, L.R.B.; Rodrigues, V.P.; Guerreiro, R.N.; Costa, D.; Câmara, M.A.R.; dos Reis Júnior, S.H.

Universidade Federal do Pará.
mareiscam@gmail.com

Human T-cell lymphotropic virus (HTLV) is part of the retrovirus family and is endemic in Japan, the Caribbean, Africa, Iran, Central and South America and the islands of Melanesia. In Brazil, the literature points to approximately 2.5 million people infected by HTLV-I, being the country with the highest absolute number of cases. Generally, studies on the epidemiology of HTLV-I consist of seroprevalence in blood donors and intravenous drug users. Thus, the objective of this study was to evaluate the frequency of blood donors, infected by HTLV virus, in a blood bank of the Brazilian Amazon region, from 2010 to 2017. **METHODS:** This is a retrospective, descriptive study whose data were collected in the Tucuruí-Pará blood bank database, organized and analyzed in Microsoft Excel 2010. **RESULTS:** During the period from 2010 to 2017 there were 17,727 donors in Tucuruí, of which, 889 (5%) were with the sample contaminated by some type of infection. Of these infections, the positivity for HTLV represents 40 samples (4.5%). **CONCLUSION:** Finally, it is concluded that the frequency of HTLV-1/2 in this study was lower than some reports in the Brazilian literature and superior to others, emphasizing the importance of the diagnosis to reduce transmission risks.

HTLV-1/2 TRENDS IN FOUR BLOOD CENTERS IN BRAZIL FROM 2010 TO 2017.

Loureiro, P.; Capuani, L.; Proietti, A.B.; Salete, C.; Gonzalez, T.T.; de Almeida-Neto, C.; Sabino, E.C.

Universidade de Pernambuco/Fundação Hemope
paula.loureiro10@gmail.com

Human T lymphotropic virus type 1/2 infection is endemic in Brazil and surveillance should be assessed. The aim of this study is to assess the prevalence of HTLV 1/2 among blood donors from the period of 2010 to 2017 in four blood centers and to characterize the trend of the infection. Methods: Population – blood donors. Serological tests- Elisa was performed in all blood samples. Statistical analysis: Prevalence and 95% confidence intervals for first time donations were calculated by year, socio demographic characteristics, type of donation, and location. We used all first time donations repeatedly positive for HTLV plus all probable first time donations positive on screening by one EIA. We used 139/216 probability that a first time donation only tested at screening would be positive in the confirmatory test. A two-sided p-value < 0.05 was considered to be statistically significant. Results: Total of 983.084 thousand of blood donations were analysed, among them 1622 samples were confirmed to be seropositives, representing a prevalence of 165/100.000 donations. The age range varies from 20 to plus 50 but the most frequently positive cases were from 20 to 39 age range. Females are predominant, 51,5% overall the positive cases. Mixed color population is more frequent. Replacement donations are more frequently associated with positives cases than Community. The Hemocenter in Recife represents 39,8% of the total positive donations. The trend from 2010 to 2017 in all centers does not change a lot and maintain almost the same prevalence each year. Conclusion: The HTLV 1/2 infected blood donors occurred every year in the period without significant yearly variance. The screening for transmissible infections among blood donors showed that this infection for HTLV-1/2 has been maintained in the last decade in diverser regions and the trend among blood donation in the seven years evaluated has shown it very clearly. The monitoring of HTLV-1/2 seroprevalence in blood donors must be sequentially assessed and others strategies should be implemented to reduce the viral infection among the population.

INFODEMOLOGY OF HUMAN T-CELL LYMPHOTROPIC VIRUS USING GOOGLE TRENDS.

Fernandes, D.M.; Lima, S.B.A.; de Carvalho, C.A.M.

Famaz
danielamafra18@gmail.com

Introduction: Human T-cell lymphotropic virus (HTLV) is responsible for adult T-cell leukemia/lymphoma, affecting 15-20 million people worldwide – a number that requires continuous updating. In this sense, internet-derived information has been recognized as a viable surrogate tool for estimating epidemiology and gathering data about patterns of disease. Objectives: Measure recent global public interest in HTLV by digital epidemiology, identifying the leading countries and subregions. Methods: Web searches for HTLV in the period from July 1st, 2016, to June 30th, 2018, were analyzed on Google Trends, limiting to the health category and including regions with low search volume. Results: HTLV was more popular in French Guiana, Jamaica, Peru, Brazil and Martinique. In the last four countries, the popularities of this search term were 87%, 73%, 66% and 54% of that in French Guiana, respectively. In Brazil, Bahia led the popularity of HTLV in web searches, followed by Pará, Distrito Federal, Mato Grosso do Sul and Pernambuco with 45%, 41%, 40% and 35% of the popularity in Bahia, respectively. Conclusion: Data on HTLV measured by Google Trends significantly correlated with those from traditional health surveillance systems, suggesting that such internet query platform may be potentially used to identify outbreaks and guide intervention strategies.

MORBIDITY PREVALENCE IN HTLV-1 INFECTED INDIVIDUALS WITH NEUROLOGICAL FOLLOW-UP IN GIPH COHORT.

Romanelli, L.C.F.; Ribeiro, M.A.; Ferreira, A.S.D.; Gonçalves, D.U.; Starling, A.L.B.; Carneiro-Proietti, A.B.F.; Martins, M.L.

Fundação Hemominas, Belo Horizonte, Brazil.
lcfromanelli@yahoo.com.br

The morbidity associated with HTLV-1 infection remains unclear and HAM is the classic and the most severe neurological impairment. Objective: To assess the prevalence of HAM and other morbidities in HTLV-1 infected individuals during their neurological follow-up by GIPH. Methods: We considered all participants who underwent neurological evaluations from 2007 to 2017 (n=334). Prevalence was calculated considering the last neurological evaluation. We exclude morbidities associated with other etiologies. Results: The mean age of individuals (n=334) was 47 (\pm 14) years and 63 % were female (n=210). HAM prevalence (n=39) was 12%, mean age was 48 (\pm 13) years and 79% were female (n=31). The morbidities observed with higher prevalence than HAM were: low back pain (n=97, 29%), fatigue (n=85, 25%), urinary dysfunction (n=80, 24%), cramps (n=76, 23%), intestinal constipation (n=69, 20%), myalgia (n=56, 17%) and sexual dysfunction (n=51, 15%). The prevalence of other diseases possibly associated with HTLV-1 infection were: arthritis or vitiligo (n=5, 1.5%), uveitis or dry eye (n=3, 0.9%), leprosy (n=2, 0.6%) and strongyloidiasis (n=1, 0.3%). The rate of individuals with HTLV-1 associated morbidities was 22% (n=74). Conclusion: HTLV-1 morbidity had an important frequency in HTLV-1 carriers followed by GIPH and although these patients do not meet the criteria for HAM, these morbidities bring important impairment in their quality of life.

NEUROLOGICAL DISABILITY AND DEPRESSIVE SYMPTOMS OF PATIENTS WITH TROPICAL SPASTIC PARAPARESIA / MIELOPATHY ASSOCIATED WITH HTLV-1.

Balieiro, J.J.; Tavares, K.N.F.; de Andrade, A.A.S.; de Souza, L.B.R.; Fonseca, Y.M.; Fampa, S.G.C.O.; do Nascimento, D.C.S.; Silva, D.C.; Normando, V.M.F.; da Cunha, B.C.S.; Pinto, D.S.

Universidade Federal do Pará
ulianabalieiro.13@gmail.com

INTRODUCTION: Tropical Spastic Paraparesis / HTLV-1 Associated Myelopathy (HAM/TSP) is one of the main neurological manifestations associated with the HTLV-1. This study aims to analyze the neurological incapacitation (IN) and the depression of patients with HAM/TSP. **METHODS:** A case series study was carried out with symptomatic HAM/TSP patients. Two evaluative instruments, EIPEC-2 and Beck Depression Scale, were applied. Under opinion number 063/2011-CEP / NMT. **RESULTS:** Ten patients, 7 women and 3 men, mean age 58.1 years, were included in the study. The first variable, IN degree, obtained a mean score of 9.4 points, the lowest score was 2 and the highest was 17 points, according to the IPEC-2 scale, the higher the score was the higher the IN, and it could reach 34 points. In the evaluation of depressive symptoms, results ranged from 3 to 43 points, 60% did not present any depression, while 40% indicated some degree of depression, 1 patient had mild depression, 2 moderate and 1 severe. **CONCLUSION:** IN and depression in patients with HAM/TSP were altered, suggesting clinical relevance for interventions in this population. Further research is needed with a greater number of subjects to identify the real IN and depressive symptom afflictions in this population.

PHYSIOTHERAPY INTERVENTION IN BODY BALANCE AND GAIT IN HUMAN T-LYMPHOTROPIC VIRUS TYPE 1 ASSOCIATED MYELOPATHY.

da Cunha, B.C.S.; Balieiro, J.J.; da Silva, D.C.; da Costa, S.G.C.O.V.; Tavares, K.N.F.; Pinto, D.S

Universidade Federal do Pará (UFPA)
biancafisioufpa@gmail.com

Human T-lymphotropic virus type 1 (HTLV-1) -associated myelopathy / tropical spastic paraparesis (HAM / TSP) is a chronic inflammatory disorder of the spinal cord. HAM/TSP patients often experience difficulty in locomotion and loss of body balance. These symptoms may impair the performance of their mobility / locomotion. In this way, this study is developed with the objective of investigate the effectiveness of the physiotherapy intervention in body balance and gait these patients. Methods: The study is characterized by being quantitative, descriptive, of the transverse tipe, developed in 12 patients carrers HAM/TSP. Patients were submitted a physiotherapy rehabilitation protocol of 15 sessions. Body balance and gait disturbances were evaluated by Tinnet Index and Time Get Up and Go (TUG). Results: In the evaluation of body balance, the means of the final results are little different from the initial ones, with a slight improvement in the Tinetti domain and balance. In the evaluation of mobility, the scores obtained in the final result were higher than the initial scores, with a positive repercussion on the mobility of these patients ($p=0,0241^*$). Conclusion: Physiotherapy may improve the symptoms of patients with HAM/TSP, both maintaining its function and improving it, thus acting positively on its functionality.

PREDOMINANCE OF HTLV-2A/C INFECTION IN ENDEMIC AREA OF THE BRAZILIAN AMAZON.

Silva, I.C.; Nobre, A.F.S.; de La-Roque, D.G.L.; Pereira, C.C.C.; de Araújo, M.W.L.; Covre, L.S.C.; Viana, M.N.S.A.; dos Santos, L.P.M.; Ferreira, M.A.S.; da Costa, C.A.; Casseb, S.M.M.; de Sousa, M.S.

Universidade Federal do Pará/Programa de Pós-graduação de Doença.
ingridchristiane22@gmail.com

Background: Human T-Lymphotropic Virus 2 (HTLV-2) is a retrovirus which is endemic among amerindian populations, pygmy tribes and mongolian people, and users of injectable drugs in the United States, Europe and Asia. The amazon region has been found to be the most endemic region in the world for HTLV-2, which was found in 17 out of 26 of the amerindian investigated communities. The metropolitan region of Belém is an endemic area for HTLV infection, presenting high frequency of vertical intrafamily transmission for HTLV-2. Although not presenting major morbidity, epidemiological surveillance studies for this infection have been of great importance. The objective of this study is the evaluation of the epidemiological aspects of HTLV-2 infection in an endemic area of the brazilian amazon region. Methods: This is a retrospective study with individuals infected by HTLV-2 (index cases) referred to a federal health education unit between 2008 and 2018 and their relatives. Viral HTLV-2 subtypes were identified by means of molecular investigation of HTLV env region, as well as their intrafamilial transmission frequency. Results: The 27 investigated index cases covers subjects with average age of 51.2 years old, with 55.5 percent of female cases (15/27) and 70.4 percent (19/27) coming from blood bank. For those who answered the socio-epidemiological questionnaire, 80 percent (16/20) were married, 78.6 percent (11/14) were self-declared brown or black skin, 73.7 (14/19) had no history of blood transfusion, 100 percent (18/18) declared not to use injectable drugs, 100 percent (19/19) declared to be heterossexuals, 63.2 percent (12/19) declared to have a monthly average family income of U\$ 250 and 52.9 percent (9/17) declared to have attended school for 10-12 years. The HTLV-2A/C subtype was present in 100 percent (27/27) of the investigated individuals. Possible intrafamilial transmission cases occurred in 63 percent (17/27) of the investigated families. Among 17 marital relationships and 10 mother-and-child relationships, sexual and vertical transmission probably occurred in 64.7 percent (11/17) and 60 percent (6/10) of the cases, respectively. Conclusion: Predominance of HTLV-2A/C subtype might be associated with dissemination of the infection by native amerindian people, and mainly due to expressive intrafamilial transmission.

PROPOSAL OF LINE OF CARE FOR PEOPLE CONVIVING WITH THE HUMAN T-CELL LEUKEMIA VIRUS (HTLV) IN THE STATE OF BAHIA - A REPORT OF EXPERIENCE.

dos Anjos, L.C.; Boullosa, M.A.R.

Secretaria da Saúde do Estado da Bahia.
lcdafisio@gmail.com

The implementation of the right to health in Brazil, as described in the Constitution, depends on overcoming inequalities, since the national context is marked by deep socioeconomic problems, with serious repercussions for health policies. In the case of HTLV virus infections, there is a problem of difficult technical-scientific solution and still little contemplated in the scope of the policies. **OBJECTIVE.** The objective of the present study is to report the experience of the Bahia State Health Secretariat (SESAB) in confronting HTLV, as well as to present the proposal of the Line of Care (LC) to people living with the virus in the state of Bahia. **METHOD.** This is an experience report, describing the process and method of LC construction. **RESULTS.** The construction of the LC found several difficulties, such as lack of scientific evidence to support management decisions, lack of knowledge about the virus by health professionals, unaware of HTLV by the population, lack of specific drugs for the treatment, lack of consensus on childbirth and breastfeeding. **CONCLUSION.** The implementation of the LC will represent an invaluable advance in the attention to Brazilian Unified Health System (SUS) users, and may serve as a model for future experiences in other states.

SOCIAL AND ENVIRONMENTAL CHARACTERISTICS OF WOMEN INFECTED WITH HTLV-1 VIRUS IN BELÉM.

de Andrade, A.A.S.; do Nascimento, D.C.S.; Lemos, C.I.L.; de Souza, L.B.R.; Pinto, D.S.

Universidade Federal do Pará (UFPA)
andrezaandrade@live.com

Type 1 lymphotropic virus (HTLV-1) is a delta retrovirus of worldwide distribution and Brazil hosts 800 thousand people infected with this virus. Objective: To verify the social and Environmental characteristics of female patients infected with HTLV-1. Methods: This is a documentary study, in which 112 medical records of HTLV-1 patients treated at the Laboratory of Clinical and Epidemiology of Endemic Diseases of the Nucleus of Tropical Medicine of the Federal University of Pará, from 2000 to 2016, were verified. The research was initiated after the approval of the Ethics and Research Committee of the University Hospital João de Barros Barreto, with registration number: 2,026,582. Results: The average age was 51 years, with the marital status being: 43.75% Single, 42.85% Married, 9.9% Widowed and 3.5% Divorced. On average, these women have been living with the virus for 8 years. And 67.85% had their diagnosis by the Center Foundation of Hemotherapy and Hematology of Pará (HEMOPA), with approximately 81.25% of the asymptomatic and 18.75% symptomatic patients for tropical spastic paraparesis / myelopathy (TSP / HAM). Conclusion: The study evidenced the predominance of women with HTLV-1 over 40 years and asymptomatic for TSP / HAM.

SOROLOGICAL AND MOLECULAR PROFILE OF HTLV 1/2 DETECTED IN THE SCREENING OF BLOOD DONORS IN THE PERIOD FROM 2014 TO 2017 AT THE HEMOPA FOUNDATION.

Monteiro, L.A.; Rodrigues, S.V.; Macêdo, J.M.O.; Barroso, C.F.; do Nascimento, L.N.S.; Miranda, D.L.C.; Barile, K.A.S.; Amaral, C.E.M

Universidade do Estado do Pará (UEPA), Belém, Brasil, Fundação C. lyne-monteiro@hotmail.com

Since 1993, screening for human T-cell lymphotropic virus (HTLV) 1/2 in blood donors is mandatory in Brazil, because this virus could be transmitted through blood transfusion. This study purposed correlate results of screening and confirmatory tests. The data were obtained in the Blood Bank System (SBS and SBS web) from the serological screening of HEMOPA Foundation's donors from August 2014 to December 2017 considered inapt in chemiluminescence test (ARCHITECH rHTLV1/2). Samples with $S / CO > 0.8$ were considered reagent. Confirmation was performed from qPCR using TaqManR system. During the period, 610 samples were reagent in the serological screening for anti-HTLV 1/2. 220 (36%) presented an S/CO ratio between 0.8 and 1.2, and 390 (64%) presented a S/CO ratio > 1.2 . In all samples, qPCR was performed as confirmatory test. There was viral genome detection in only 129 (33%) of 390 samples with $S/CO > 1.2$. About the 129 detectable samples, 103 were HTLV-1 (80%) and 26 HTLV-2 (20%), evidencing HTLV-1 being the predominant type in our sample number. Nearly 70% of the reactive samples in serological screening correspond to a possible false-positive result, emphasizing the importance of combined interpretation of the tests.

SURVEILLANCE AND PREVENTION OF INFECTIONS AND ASSOCIATED DISEASES WITH THE HUMAN T-CELL LYMPHOTROPIC VIRUS IN BELÉM, PARÁ, BRAZIL.

dos Santos, L.P.M.; Coelho, J.L.; Silva, I.C.; Pinheiro, B.T.; Almeida, D.S.; Nobre, A.F.S.; Bastos, L.S.S.; Covre, L.S.C.; de Araújo, M.W.L.; Viana, M.N.S.A.; da Costa, C.A.; Ferreira, M.A.S.; de Sousa, M.S.

Universidade Federal do Pará.
lyzandrapmsantos@gmail.com

HTLV infection has been reported in all South American countries, presenting different prevalence rates. In Brazil, the state of Pará stands out as the third most prevalent among blood donors. This study aims to describe epidemiological results from HTLV infection obtained during five years of surveillance in the city of Belém, capital of the state of Pará. **METHODS:** During university extension actions, from January 2013 to December 2017, serological searches for anti-HTLV-1/2 antibodies and detection of provirus DNA using nested-PCR were performed. **RESULTS:** In this period, 3229 people with an average of 40.9 years were investigated, 71% being female. Surveillance activities detect 53.7% cases in active searches, 42.8% in university reference unit, and 3.5% were attended by spontaneous search. The anti-HTLV-1/2 antibody was observed in 8.6% (277/3229) of the investigated patients, corresponding to 13.8% (191/1385) of the cases in the reference unit, 4.8% (84/1733) of those investigated by active search and 1.8% (2/111) of those investigated by spontaneous demand. HTLV-1 infection was confirmed in 8.8% (122/1385) of the referenced cases and 3.3% (58/1733) in active search cases. HTLV-2 infection was confirmed in 1.8% (25/1385) cases, 0.6% (11/1733) in active search cases and 0.9% (1/111) in spontaneous demand. The frequency of infection was significant among women (8.3%), who had a mean age of 46 years. **CONCLUSION:** It was observed in this study a high prevalence of HTLV infection in active demand searches, confirming the city of Belém as an endemic area, pointing out the importance of actions aimed at improving the investigation process of the virus carriers.

THE RELATION OF DIZZINESS SYMPTOM WITH THE HTLV-1 INFECTION: A SISTEMATIC REVIEW.

de Souza, L.B.R.; do Nascimento, D.C.S.; de Andrade, A.A.S.; Pinto, D.S.

Universidade Federal do Pará.
brynneleonard@hotmail.com

Dizziness is a symptom often related by the patient who sees all objects around him spinning, triggering loss of functionality and indicating involvement of intracranial structures, something uncommon for HTLV-1 patients, asymptomatic or symptomatic for Tropical Spastic Paraparesis. Nevertheless, the informations connecting dizziness and HTLV-1 on literature are dispersed and scarce. Objectives: Establish the relation of dizziness symptom with the HTLV-1 infection. Methods: This is a sistematic review, based in PUBMed, PUBMed Health, PMC, MEDLine, Lilacs, Bireme, Scielo, Scopus, databases. It was decided to include only english articles to the research. The key-words were: “HTLV-1 vertigo, HTLV-1 dizziness, HTLV-1 stagger, HTLV-1 vestibular alterations”. The articles included were published in scientific papers with impact factor superior to 1,300 with publication’s date posterior to 2013 and necessarily had to add symptomatic and asymptomatic patients. It started with 23 articles, but it was only included 3. Results: All the studies showed HTLV-1 infection increased the possibility of vestibular and neurological damage and, so, the appearance of dizziness, in symptomatic and asymptomatic patients. Conclusion: Exists a relation between the appearance of dizziness symptoms with infection by HTLV-1.

THE ROLE OF METHALOPROTEINASES (MMP) -3, MMP-9 AND S100B IN THE PATHOGENESIS OF HTLV-1 INFECTION.

Guerra, M.; Carvalho, N.; Santos, S.; Carvalho, E.M.; Carvalho, L.P.

Universidade Federal da Bahia.
marieleguerr@hotmail.com

Introduction: The MMPs are enzymes that affect blood-brain barrier (BBB) integrity which would facilitate the migration of cells present in the blood into the CNS. The S100B is observed in cases with death astrocyte. The aim of this study is to evaluate the importance of MMP and S100B in the pathogenesis of HTLV-1 infection. Methods and Results: The MMP-3, MMP-9 and S100B were measured by ELISA in serum and cerebral spinal fluid (CSF) of the HTLV-1 infected. In the serum, the levels of the MMP-3 in patients with HAM/TSP were significantly lower when compared with HTLV-1 carrier, $p=0.01$. The concentrations of MMP-9 in HTLV-OAB were lower when compared to HAM/TSP, $p=0.0002$, and HTLV-1 carrier, $p=0.007$. The levels of S100B, in serum, didn't have difference between the groups, but in CSF had difference between HTLV-OAB and HAM/TSP, $p=0,03$. Conclusion: The involvement of MMPs in the process of destruction of the BBB is not yet clear. It is necessary to analyze the inhibitors of metalloproteinases (TIMP-3 and TIMP-4). The possible explanation for the low MMP-3 levels observed in serum from HAM/TSP patients is the probable consumption of this protein leading to BBB destruction of these individuals.

THERAPEUTIC EFFECT OF THE PILATES METHOD IN THE ESFINCTERIAN FUNCTION OF PEOPLE WITH HAM / TSP: RANDOMIZED CLINICAL TRIAL.

Nunes, R.F.R.; da Fonseca, E.P.; Leme, A.P.C.B.P.; Souza, C.R.J.; Sousa, M.C.M.; Menezes, N.S.; Pinto, E.B.; Sá, K.N.

Católica University of Salvador
reebecaa.nunes@hotmail.com

HTLV-1 Associated Myelopathy / Tropical Spastic Paraparesis (HAM/TSP) is an inflammatory condition, predominantly involving the spinal cord. It results in progressive and incapacitating signs and symptoms as sphincter control. The objective was to verify the therapeutic effect of Pilates on the sphincter function of people with HAM / TSP. Methods: Randomized clinical trial. Included individuals with a diagnosis of HAM / TSP, of both genders, from 18 to 64 years. Excluded individuals with psychiatric disorders, pregnancy, rheumatic or orthopedic diseases, other neurological conditions or with difficulty of understanding. The test group (TG) performed the Pilates and the control (CG) task-oriented training. We used Agachan, Wexner and bladder hyperactive (OABSS) scales. Results: Wexner varied in the CG from 1.5 to 1.0 (0.0-0.6) (P= 0.750) and in the TG from 0.0 (0.0-5.0) to 1.0 (0.0-6.5) (P = 1,000). In Agachan, CG was 9.5 (5.5-12.7) to 12.5 (7.7-15.2) (P=0.188), in the TG of 6.0 (2.0-11 , 5) to 9.0 (2.5-12.0) (P=0.625). The OABSS in the CG of 3.0 (1.0-11.0) to 6.0 (4.5-10.2) (P=0.469) and in the TG of 9.0 (5.0-10.5) to 7.0 (4.0-9.5) (P=0.750). Conclusion: Method Pilates reduced urinary symptoms in people with HAM / TSP despite the absence of statistical evidence.

TRANSCRIPTIONAL FACTOR ARYL HYDROCARBON RECEPTOR (AHR) EXPRESSION AND ITS CORRELATION TO Th17 AND T REGULATORY CYTOKINES IN HTLV-1 INFECTED PATIENTS.

Lopes, W.A.M.; do Nascimento, E.G.; Rodrigues Júnior, R.S.; Pedroza, L.S.R.A.; Gomes, J.A.N.; Yoshikawa, G.T.; Fujihara, S.; Koyama, R.V.L.; Dias, G.A.S.; Sousa, R.C.M.; Quaresma, J.A.S.; Fuzii, H.T.

Universidade Federal do Pará.
wesley.nart90@gmail.com

Human T-cell leukemia virus type 1 (HTLV-1) infects 5-10 million people and is related with HTLV-1 associated myelopathy/tropical spastic paraparesis (HAM/TSP). In HTLV-1 infected patients, it is known that there is an imbalance between pro-inflammatory and regulatory factors with an exacerbation of the former. Therefore, transcriptional factors such as aryl hydrocarbon receptor (AHR) may play an essential role. Furthermore, HTLV-1 infects mainly T CD4+ cells. Those cells can generate pro-inflammatory (Th17) or regulatory cells [Tregulatory (Treg)]. Finally, AHR favors the differentiation into Th17 and Treg cells. Therefore, we aim to expand the knowledge about the correlation between AHR and the cytokines of Th17 (IL-17) and Treg (IL-10) responses in HTLV-1 infected patients. Methods: In this study 68 HTLV-1 infected patients were included from whom 34 patients were asymptomatics, 11 oligosymptomatic, and 23 patients with HAM/TSP. We used relative expression of IL-17, IL-10 and AHR from peripheral blood samples of HTLV-1 infected patients using real time PCR. The formula $2^{-\Delta CT}$ (where $\Delta CT = CT_{\text{gene}} - CT_{\text{constitutive gene}}$) was used to estimate the expression of the cytokines. GAPDH and β -actin are the constitutive genes Results: AHR expression was increased in HAM/TSP patients with no differences among groups (Kruskal-Wallis, $p = 0.2672$). IL-17 expression was similar in all groups (Kruskal-Wallis, $p = 0.4240$) with lower expression in oligosymptomatic patients. There were significant differences (Kruskal-Wallis, $p < 0.0001$) among the patients regarding the expression of IL-10. IL-10 expression in asymptomatic patients was significantly increased when compared with both oligosymptomatic patients (Mann-Whitney, $p = 0.0010$), and HAM/TSP patients (Mann-Whitney, $p < 0.0001$). Regarding the correlations, there was a moderate negative correlation between AHR x IL-10, and moderate positive correlation between AHR x IL-17 in HAM/TSP patients, both were non-significant. In the Oligosymptomatic patients, the correlation between AHR x IL-17 was moderately positive while the other correlations were insignificant. Asymptomatic patients presented moderate positive correlation and statistically significant between AHR x IL-17. Finally, the correlation between IL-10 and IL-17 was insignificant. Conclusion: AHR may play a more significant role in pro-inflammatory responses (Th17) among all HTLV-1 infected patients.

VARIATION OF THE SPIROMETRIC RESPONSE IN HUMAN T-LYMPHOTROPIC VIRUS TYPE I (HTLV-I) CARRIERS.

Normando, V.M.F.; Dias, A.R.N.; Dias, A.M.L.; Teixeira, I.S.; de Oliveira, P.B.; Falcão, L.F.M.; Pinto, D.S.; Quaresma, J.A.S.

Federal University of Pará.
valeriafisio@gmail.com

The respiratory system may be the target of damages resulting from human lymphotropic virus type I (HTLV-I) infection, which may impair its functional activities. This study aimed to compare predicted spirometric values obtained in HTLV-I virus carriers of both sexes. **Materials and Methods:** A cross-sectional study was carried out in the Laboratory of Studies in Functional Rehabilitation of the Federal University of Pará (Opinion no. 2106481), from October 2017 to January 2018. We evaluated 11 individuals (07 women and 04 men) of HTLV-I virus with HAM-TSP and asymptomatic for lung diseases. Spirometry was performed according to the standards of the Brazilian Society of Pneumology and Tisiology, using reference values for forced maneuver in white adult Brazilians. **Results:** The T-test for paired samples revealed significant differences between predicted values for VC ($p = 0.007$), FEV1 ($p = 0.03$), FEFmax ($p = 0.01$), FEF75% (0.05) for females and FEFmax ($p = 0.04$) for males. **Conclusion:** The study points to a decrease in pulmonary function values in the virus carriers, predicting the need for follow-up against possible damage to the respiratory system.

ADULTHOOD INFECTIVE DERMATITIS ASSOCIATED WITH HTLV-1: EVALUATION OF 11 CASES.

Souza, L.S.¹; Silva, T.S.²; de Oliveira, M.F.P.²; Farré, L.³; Bittencourt, A.L.¹

1. Pathology Service, Prof. Edgard Santos Teaching Hospital, Federal University of Bahia, Salvador, Bahia, Brazil

2. Department of Internal Medicine, Prof. Edgard Santos Teaching Hospital, Federal University of Bahia, Salvador, Bahia, Brazil

3. Laboratory of Experimental Pathology, Gonçalo Moniz Research Center, Oswaldo Cruz Foundation (CPQGM/FIOCRUZ), Salvador, Bahia. ProCURE Program, Catalan Institute of Oncology, l'Hospitalet de Llobregat, Barcelona, Spain.

lucasouza16@gmail.com

Infective dermatitis associated with HTLV-1 (IDH) is a severe form of childhood eczema. Progression of juvenile IDH to HTLV-1 associated myelopathy (HAM) occurs in 54% of IDH cases, in Bahia, Brazil. Only eleven cases of adulthood IDH have been published. In the present study we intend to evaluate the clinico-pathological and molecular aspects of adulthood IDH comparing them with the juvenile form. **MATERIALS AND METHODS:** Eleven patients were included. Diagnosis was performed according to Oliveira et al,2012. HTLV-1 infection was detected by ELISA/Western blot. Proviral load (PVL) was performed in eight patients using quantitative PCR considering HTLV-1 tax region. **RESULTS:** The lesion's distribution and morphology, and histopathological/ immunohistochemical aspects were similar to those of juvenile IDH. Five patients had association with HAM/TSP, in three IDH occurred after HAM/TSP. PVL was as high as the PVL of juvenile IDH. **CONCLUSION:** Clinico-pathological/immunohistochemical aspects and PVL levels of adulthood IDH were similar to those observed in juvenile IDH. Frequency with HAM/TSP association was high (45%), similar to that observed in juvenile IDH (54%). The current study confirms that IDH diagnostic criteria can also be applied to adulthood IDH. Different from the juvenile form, IDH may appear after the development of HAM/TSP.

THE IMPACT OF MAT PILATES ON THE RESULTS OF VENTILATORY TESTS IN HUMAN T-LYMPHOTROPIC VIRUS TYPE 1 (HTLV-1) CARRIERS.

Normando, V.M.F.; Dias, A.R.N.; Dias, A.C.L.; Balieiro, J.J.; Furtado, K.N.T.; Fonseca, Y.M.; Falcão, L.F.M.; Pinto, D.S.; Quaresma, J.A.S.

Universidade Federal do Pará
Universidade Estadual do Pará
valeriafisio@gmail.com

Human T lymphotropic virus type 1 (HTLV-1) infection may compromise pulmonary mechanics. Exercises directed to abdominal isotonic contractions and breathing control may have an impact on lung function and quality of life. The study aimed to verify the influence of Mat Pilates on pulmonary mechanics through respiratory awareness in patients with HTLV-1. **Materials and Methods:** A longitudinal study was carried out in the Laboratory of Functional Impacts Studies of the Federal University of Pará (Opinion no. 2106481) through a Mat Pilates protocol, twice a week, in the morning shift, reinforcing the focus of diaphragmatic respiratory awareness. Eleven (07 women and 04 men) HTLV-1 carriers with HAM-TSP and asymptomatic for lung disease, performed pulmonary function tests in the years 2013 and 2018. **Results:** Women: VC ($p=0.004$), FEV1/FVC ($p=0.001$), FEF25-75% ($p=0.005$), TEF25-75% ($p=0.000$), FEF50% ($p=0.005$), FEF75% ($p=0.008$). Men: FEV1/FVC ($p=0.02$), FEF25-75% ($p=0.03$), TEF25-75% ($p=0.00$), FEF75% ($p=0.01$). **Conclusions:** There was an improvement in volumes, capacities and flows for both sexes when using the Mat Pilates method, as an important therapy for respiratory awareness in patients with HTLV-1.

HEMATOLOGICAL CHANGES IN PATIENTS WITH HUMAN T-LYMPHOTROPIC VIRUS 1.

Sousa, M.S.; Ribeiro, J.F.; Covre, L.S.C.; Silva, I.C.; Nobre, A.F.S.; Borges, M.S.; Almeida, D.S.; Costa, C.C.

Univerisidade Federal do Pará.
jairbiocenter@gmail.com

Human T-lymphotropic virus 1 (HTLV-1) progresses slowly, with the risk of developing associated disease. In Brazil it is estimated that more than three million people are infected with HTLV-1 and Belém do Pará stands out as one of the endemic regions for infection. The association between HTLV-1 infection and haematological disorders, which may progress to malignancy, makes the hematological evaluation of infected patients important. This study demonstrates the hematological profile, with the frequency of lymphocytic atypia, of HTLV-1 infection in an endemic area of the Brazilian Amazon.

METHODS: Hematologic parameters evaluation, lymphocytic atypia research and evaluation of the profile of individuals attended at a health educational unit in Belém, in the period from May 2015 to August 2016, after their consent. Hemograms were obtained from all blood samples collected from patients and the blood smear was made for staining through Leishman stain and differential leukocyte count. **RESULTS:** total of 202 individuals were investigated, of which 87 had HTLV-1 infection (most of the hemotherapy center) and 115 were uninfected (most of them infected). Significantly higher prevalence (71.3%, $p = 0.0090$) of the infection was observed in women. The mean age of the infected individuals (46.5 years) was higher than the non-infected ones (40.3 years) ($P = 0.0094$). Those infected by HTLV-1 did not show a significant change in the overall leukocyte count ($p = 0.0731$). The analysis of hematological parameters presented a higher proportion of eosinophils (4%, $p = 0.0239$) and a lower proportion of the segmented ones (54%, $p = 0.0123$) in HTLV-1 carriers. Lymphocytic atypical was present only in patients with HTLV-1 ($p = 0.0001$), with a frequency of 20.7%. **CONCLUSION:** It is concluded that HTLV-1 infection stands out in women over 50 years. The hematological profile of those infected shows a reduction of segmented, an increase of eosinophils and the presence of atypical lymphocytes. The hematological profile of the HTLV-1 carrier should always be evaluated to identify early some diseases associated with infection.

EVALUATION OF THE TH9 PROFILE IMMUNOLOGICAL RESPONSE IN PATIENTS INFECTED WITH HTLV-1.

Gomes, J.A.N.; dos Santos, L.C.; Rodrigues Júnior, R.S.; Sousa, R.C.M.; Quaresma, J.A.S.; Fuzii, H.T.

Universidade Federal do Para.
jessicaang13@gmail.com

HTLV-1 is associated with HAM/TSP, inflammatory disease, linked to the immune response, demyelinating that affects the spinal cord. Objectives: To evaluate the Th9 profile in HTLV-1 infected with or without HAM/TSP and to correlate with balance and gait. Methodology: RNA was isolated from HTLV-1 infected patients blood, Gene expression of IL-9, PU. I and IRF-4 was performed using qPCR with GoTaq qPCR kit. Gene expression was calculated by $2^{-\Delta\Delta CT}$. Tinetti balance scale and gait evaluation were evaluated. Results: From 49 HTLV-1 infected patients, 12 (24.49%) presented HAM/TSP, 8 (16.33%) were oligosymptomatic and 29 (59.18%) asymptomatic. The mean expression of IL-9 in HAM/TSP (0.001947) and in oligosymptomatic (0.00050228) were lesser than what was seen in asymptomatic (0.011049862), but not significant ($p = 0.4069$). For PU. I and IRF-4 expressions, all groups showed the same mean. IL-9, PUI and IRF-4 presented a positive correlation with the balance, $r = 0.6079$, $r = 0.2286$ and $r = 0.2055$, respectively. Correlation between gait and expressions of IL-9, PU. I and IRF-4 was negative. Conclusion: It has been shown that IL-9 is less expressed in HAM/TSP and oligosymptomatic patients than in asymptomatic patients and its expression seems to be protective to symptoms development.

CLINICAL AND SEROEPIDEMIOLOGICAL EVALUATION OF HTLV-1/2 INFECTION OF PATIENTS ATTENDED AT THE EVANDRO CHAGAS INSTITUTE DURING THE PERIOD OF 2000 TO 2015.

Lima, I.T.; Linhares, A.C.; Macedo, O.; de Moura, A.; dos Reis, R.M.; de Freitas, R.C.A.; Freitas, F.B.

Instituto Evandro Chagas/SVS/MS.
igortenorio003@gmail.com

Introduction and Objective: Although the geographical distribution is well established, there are several variations in the prevalence of HTLV-1/2 in different regions and specific population groups. Approximately 90% of the patients will remain asymptomatic throughout their lives. However, the infection has strong associations with adult T-cell leukemia (LLcTA), HTLV 1/tropical spastic paraparesis (TSP/HAM) associated myelopathy, and other associations such as dermatological and ophthalmological diseases. The objective of the study was to evaluate the seroepidemiology and the presence of diseases associated with HTLV infection in patients attended at the Evandro Chagas Institute (IEC). **Methods:** It was used as a source of information, the database of the Retrovirus Laboratory, Virology Section, which contains epidemiological and clinical information of patients referred and attended at the Medical Assistance Service (SOAMU) of IEC, over a period of 15 years (2000 to 2015). Serological diagnosis was performed through an enzyme-linked immunosorbent assay (ELISA) and confirmed by Western blotting. **Results:** During the period, 4741 samples were analyzed, with 255 (5.38%) positive, ranging from 21% (21/99) in 2002 to 2.4% (15/627) in the year of 2014. Among the positives, 35% (90) were men, 64% (162) women and 1% had no information. The most prevalent age group was 31 to 50 years (19.6%). However, similar frequencies were found among individuals above 51 (18.1%) and 60 years (16.5%), mainly from the year 2006. Only 32 obtained the information of the viral type, where 21 (66%) were HTLV-1, 8 (25%) HTLV-2 and 3 (9%) had a mixed pattern (HTLV-1 and 2). 60 (23.5%) of the positive patients had one or more clinical signs of TSP/HAM. Of these, 14 provided information of viral type, where 8 (57%) were HTLV-1, 5 (36%) HTLV-2 and 1 (7%) presented mixed pattern. Dermatological (5%) and ophthalmologic (0.8%) manifestations, severe anemia (2%) and leukocytosis (1.5%) were other clinical signs observed in positive individuals. **Conclusion:** The research found seroprevalence above the levels seen in Brazil, which is considered as low and medium in the general population. This fact underscores the importance of the constant epidemiological surveillance of HTLV infection that may be presenting underestimated prevalences in the country. In addition, the manifestation of characteristic clinical signs and symptoms should be taken into account for a possible infection by this agent.

COMPARISON OF INSTRUMENTS FOR THE EVALUATION OF FUNCTIONAL DISABILITIES IN HTLV-1 CARRIERS WITH DIFFERENT LEVELS OF NEUROLOGICAL COMPLIANCE.

de Assis, I.M.; Domingues, M.M.; Borges, M.S.; Pinto, D.S.; da Costa, C.A.; de Sousa, M.S.

Universidade Federal do Pará.
izabela_stm@hotmail.com

It is estimated at least 20 million people infected by HTLV-1 in the world and 5% of virus carriers developed HAM / TSP development after asymptomatic phase. A set of functional safety measures is used for the evaluation, but still a series or a worsening in the patient's clinical picture. The objective of this study was to compare the EDSS, OMDS and EIPEC-2 evaluation tools with a purpose of analysis of the indication of previous tools for groups of different levels of neurological impairment carriers of HTLV-1. A cross-sectional study carried out in March 2017 with 94 patients with anti-HTLV and HTLV-1 infection by molecular biology methods, divided into 4 groups in order of decreasing neurological knowledge for HAM / TSP: Defined for HAM / TSP (Group 1 = 12), Possible for HAM / TSP (Group 2 = 13), No HAM / TSP (Group 3 = 38), Control (Group 4 = 31). During the collection period, 94 patients were evaluated, 59 (62.76%) women and 35 (37.23%) men, among them. The mean age was 48.2 years: 49.0 years for women and 48.3 years for men, with a difference between the means of both sexes ($p < 0.0012$). As for neurological impairment, mean age was 52 years in Group 1, 47 in Group 2, 51 in Group 3 and 43 in Group 4.: 5.3 (± 5.9) points for EIPEC-2, 1, 1 (± 2.7) points for the OMDS, 1.1 (± 2.0) points for the EDSS. This is the objective of a greater precision of the first instrument, EIPEC-2, to measure the neurological incapacities within reach of the others. The correlation between the evaluations was also evaluated. The relationship between EIPEC-2 and EDSS was very significant ($p < 0.0001$), as well as between EIPEC-2 and OMDS ($p < 0.0001$). Comparing the search results on the EIPEC-2 scale with those of the OMDS and EDSS in the groups with different levels of neurological impairment, we observed the significant difference at all levels, obtaining $p < 0.0001$ for Groups 1, 3 and 4, and $p = 0.0002$ for Group 2. EDS, with the objective of evaluating EDSC-2 and the OMDS and EDSS scales, was able to be adequately evaluated for the neurological evaluation of patients with HTLV-1, with promising use of non-diagnosis and early treatment of HAM / TSP.

EVALUATION OF THE LEVEL OF KNOWLEDGE OF THE BELÉM POPULATION ON HUMAN T-CELL LYMPHOTROPIC VIRUS (HTLV).

Lopes, F.T.; Abreu, I.N.; Pereira, L.M.S.; Cayres-Vallinoto, I.; Puccioni-Sohler, M.; Vallinoto, A.C.R.

Institute of Biological Sciences, Federal University of Pará, PA.
isabella.nogueira@outlook.com.br

Human T-cell lymphotropic virus (HTLV) is the etiological agent to HTLV-1 Associated Myelopathy/Tropical Spastic Paraparesis (HAM/TSP) and Adult T-cell Leukemia/Lymphoma, but it is still a neglected infectious disease. In this context, the objective of the present study was to evaluate the level of knowledge of the population residing in Belém city about HTLV. **METHODOLOGY:** One hundred and sixteen participants were interviewed in three different shopping malls using a questionnaire that contained biological and epidemiological questions about HTLV. The data obtained were statistically analyzed using the G test and Fisher's exact test (BIOESTAT 5.3 and Graph Pad Prism 7.04). **RESULTS:** The group of interviewees was composed mainly by females (62.7%), with a mean age of 32.53 years, had a high school education (61.21%), active sex life (82.76%), who used condoms sporadically (33.62%) and who had no knowledge about HTLV (68.97%). Among those interviewed who presented prior knowledge about HTLV, those who received blood transfusion predominated ($p = 0.0026$), performed a screening test for HTLV ($p = 0.0014$) and attended the most popular shopping mall ($p = 0.0216$, $p = 0.0307$). However, this significance was not maintained in more specific questions about the biological properties of HTLV. **CONCLUSION:** Knowledge about the HTLV is still not widespread and limited to small groups, and it is necessary to implement health education measures to alert the largest contingent of people about the risks of diseases still neglected.

GENE EXPRESSION OF TRANSCRIPTION FACTORS T-BET, GATA 3 AND FOXP3 IN PATIENTS WITH HTLV-1.

Santos Júnior, J.C.M.; Yoshikawa, G.T.; Dias, G.A.S.; Sousa, R.C.M.; Quaresma, J.A.S.; Fuzii, H.T.

Universidade Federal do Pará.
juniorsantosgcj@gmail.com

Introduction: Human T-cell leukemia virus type 1 (HTLV-1) is related to HTLV-1 associated myelopathy/tropical spastic paraparesis (HAM/TSP), an inflammatory neurological disease. HTLV-1 infected patients show an inflammatory response that is the cause of CNS damage. **Objective:** To evaluate T-Bet, Gata-3 and Foxp3 gene expression to understand the immune desregulation in HTLV-1 infected patients. **Methodology:** HAM/TSP was diagnosed with WHO criteria. Blood collection from HTLV-1 infected patients and lymphomononuclear cells were separated, followed by isolation of RNA and cDNA synthesis. Gene expression was performed using qPCR with Gotaq qPCR (Promega) in Step OnePlus (Applied Biosystem). Results were analyzed by StepOne TM Software v2.0, and the gene expression was calculated using the formula 2^{-CT} , and GAPDH and b-actin like housekeeping genes. **Results:** Tbet expression were similar in HAM/TSP, oligosymptomatic and asymptomatic patients, but slightly lower in asymptomatic patients ($p = 0.86$). For Foxp3, its expression was lower in asymptomatic patients ($p = 0.7113$) and similar between oligoasymptomatic and HAM/TSP patients. For GATA-3, HAM/TSP patients presents lower GATA-3 expression in comparison to other groups ($p = 0.0826$). **Conclusion:** HAM/TSP patients showed a lower GATA-3 expression and higher T-bet comparing to other groups, so it can influence the immune response imbalance.

KEY WORDS: HTLV-1; PET/MAH; T-Bet; Gata-3; Foxp3

HTLV DIAGNOSED IN PREGNANT IN THE PERIODS OF 2014 TO 2017: AN INTEGRATING LITERATURE REVIEW.

Pimentel, H.F.S.; Galvão, R.R.G.; Dutra, D.R.F.; Wanzeler, E.L.F.; da Silva, N.P.; do Carmo, J.C.B.

Enfermeira. Docente da Universidade da Amazônia - UNAMA. Belém-PA-Brasil. Enfermeiro. Pós-Graduando pela Escola Superior da Amazônia - ESAMAZ. Belém-PA-Brasil.

Discente da Escola Superior da Amazônia - ESAMAZ. Belém-PA-Brasil.

Discente da Universidade da Amazônia - UNAMA. Belém-PA-Brasil.

hallessapimentel@gmail.com

Introdução: Human T-cell Lymphotropic Virus (HTLV) is a human retrovirus, from the same family as the Human Immunodeficiency Virus (HIV) (NASCIMENTO, 2015). The study aims to identify prevalence rates of HTLV virus in pregnant women during prenatal care. **Metodologia:** This is an Integrative Review of Literature made from Brazilian scientific publications between the years 2010 to 2018, in the Virtual Health Library (VHL), indexed in the LILACS and SCIELO database, with the following descriptors: pregnant women, HTLV and Nursing. **Resultados e Discussão:** HTLV is a virus that has not yet been adequately addressed in the literature, and health agencies have not yet mapped the correct management of prophylactic measures of this infection. Prevalence varies according to location and the main route of dissemination is vertical transmission, especially maternal breastfeeding. The regional heterogeneity of the prevalence of HTLV in Brazil is explained by the ethnic characteristics of the population, since the Northeast is the region with the highest proportion of descendants of Africans and Amerindians than the South (MELLO, 2014). **Conclusão:** All articles emphasized the importance of HTLV screening in the prenatal care setting. Health professionals should be aware of such risk factors in order to work interdisciplinarily in preventing transmission of these diseases.

HTLV-1 INFECTION AND MAJOR DEPRESSIVE DISORDER IN MODERATE OR SEVERE DEGREE: REVIEW OF LITERATURE PUBLISHED IN BRAZIL.

Cardoso, C.C.; Braga, R.R.; Neves, A.R.O.; Souza, L.G.; Magno, I.M.N.

Universidade Federal do Pará.
carinaccardoso.med@gmail.com

HTLV-1 infection can progress to HTLV-1 Associated Myelopathy/Tropical Spastic Paraparesis (HAM/TSP), which causes incapacitating conditions that can cause Major Depressive Disorder (MDD). OBJECTIVES: to unify data from the Brazilian literature that correlate HAM/TSP and clinical manifestations of MDD, moderate or severe degree. METHODS: 11 articles published between 2007 and 2018 searched on PubMed, SciELO and Scholar platforms were analyzed. 801 patients with HTLV-1 were studied, all older than 18 years. RESULTS: patients were divided into 438 HAM/TSP and 363 asymptomatic patients. These subgroups were divided by sex and by manifestation of MDD and unified in the Excel Software. Mean percentages of HAM/TSP patients by sex and by manifestation of MDD were calculated and 43.61% of HAM/TSP patients had moderate or severe MDD. Among the studies reporting genders 71.37% HAM/TSP were women. There are insufficient data about MDD in asymptomatic patients. CONCLUSION: only one study correlated sex, HAM/TSP and MDD simultaneously. Literature suggests that exists a relationship between HAM/TSP and MDD and possibly this association is more prevalent in women. However, it is a poorly explored field requiring more studies to prove the correlation between the pathologies, as well the prevalence in female population.

IMPAIRMENT OF RESPIRATORY MUSCLE STRENGTH IN PATIENTS WITH HTLV-1 ASSOCIATED MYELOPATHY IN AMAZON REGION.

Normando, V.M.F.; Dias, A.R.N.; Dias, A.C.L.; Teixeira, I.S.; de Oliveira, P.B.; Falcão, L.F.M.; Pinto, D.S.; Quaresma, J.A.S.

Núcleo de Medicina Tropical, Universidade Federal do Pará.
apiodias@gmail.com

Introduction: Patients with HTLV-1 associated myelopathy/tropical spastic paraparesis (HAM/TSP) could develop a pulmonary involvement that has been reported with radiological findings such as bronchiectasis and alveolitis, increased lymphocytes in bronchoalveolar lavage fluid analysis and dysfunctional evidence in spirometry. The aim of the study was to evaluate respiratory muscle strength in patients with HAM/TSP. **Methods:** The present study was approved by the Ethics Committee of the Federal University of Pará (no 2106481). In this cross-sectional study conducted between October 2017 and January 2018, 5 females and 9 males, with symptomatic HTLV-1 for HAM/TSP without respiratory symptoms was evaluated with a digital manovacuometer (MVD 300, Globalmed™, Arizona, USA). Data were analyzed by Graphpad Prism version 5.0 TM with α level of 0.05. **Results:** There was a reduction in muscular expiratory force for males ($p = 0.03$) and for females ($p = 0.00$), and for inspiratory muscle strength in males ($p = 0.00$). The values obtained were compared with the values predicted for both. **Conclusion:** In summary, changes in respiratory muscle strength were observed in patients with HAM/TSP, a factor that should serve as an alert for actions that avoid possible symptomatic manifestations of the respiratory tract.

KNOWLEDGE LEVEL ABOUT HTLV AMONG HEALTH PROFESSIONALS IN THE CITY OF BELÉM.

Gonçalves, L.O.; Lodeou, G.E.; de Moura, L.V.B.; Lopes, J.G.M.; Cayres-Vallinoto, I.; Puccioni-Sohler, M.; Vallinoto, A.C.R.

Universidade Federal do Pará.
loly-13og@hotmail.com

Human T-lymphotropic virus 1 (HTLV-1) was described more than 30 years ago, but still today some health professionals are unaware of the virus and its means of transmission and prevention, which makes it a neglected infectious disease. Methods: The present study evaluated the level of knowledge of 87 health professionals, residing in Belém, using a questionnaire containing eleven questions about HTLV and its properties biological, pathological, transmission routes, treatment and prevention. Results: Of the total number of professionals interviewed, 19 (22%) said had never heard of the virus. When asked about the nature of the infectious agent 13% did not know how to respond. Regarding the route of transmission, 18% reported not knowing the routes and 15% attributed saliva as a means of spreading the virus. When questioned about the relationship between HIV and HTLV, 8 (9%) said they were the same agent and 18 (21%) said they did not know. Asked about the form of diagnosis 22 (31%) of the professionals did not know to inform among the options provided in the questionnaire. Asked about HTLV-related diseases, 22% chose the AIDS option and 34% answered not knowing. Of all the professionals interviewed, nurses and nursing technicians were the ones who showed the lowest level of knowledge about HTLV. Conclusions: The results demonstrate the need to implement educational campaigns about HTLV among health professionals.

MOLECULAR DOCKING OF THE ENV PROTEIN OF HTLV-1 AND HSPG.

Coelho, R.C.C.; dos Santos, R.C.P.; Ramos, S.A.A.; Gomes, G.P.; Mendes, W.R.B.; Santos, M.E.S.; de Sousa, M.S.; Nobre, A.F.S.; Sousa Júnior, E.C.

Faculdade Integrada Brasil Amazônia – FIBRA.
rcalderarocoelho@yahoo.com.br

Human T-lymphotropic virus type 1 (HTLV-1) was the first human retrovirus discovered and is a cosmopolitan species being most often found in Japan, however, it is also present in the Middle East, South Africa, the Caribbean, in addition to presenting several cases in Brazil. This virus is associated to Tropical Spastic Paraparesis / Myelopathy. The Env protein is not well studied and some aspects remains poor described as the interaction with aminoacids of Env and HSPG. Objective: The aim of this study was to analyze the aminoacids which interacts with Env protein during the receptor binding with HSPG. Methods: For molecular docking was used the tridimensionals structures of Env protein construted by Ab Initio and HSPG, using the Autodock Vina software which uses Genetic Algorithm to define the best binding site. Results: The molecular docking show the interaction between the aminoacids: 13, 182, 271, 302-310, 319, 321-323, 325-326, 329-330 and 338. The minor energy for this system was -5.7 kcal/mol. Conclusion: The molecular docking for Env protein of HTLV-1 may help in the discovery the interactions between Env and HSPG and design of new drugs that target the HTLV.

MOLECULAR MODELING OF ENV PROTEIN OF HTLV-1 (NC_001436) BY AB INITIO STRATEGY.

dos Santos, R.C.P.; Coelho, R.C.C.; Ramos, S.A.A.; Gomes, G.P.; Mendes, W.R.B.; Santos, M.E.S.; de Sousa, M.S.; Nobre, A.F.S.; Brasil-Costa, I.; Sousa Júnior, E.C.

Evandro Chagas Institute - Department of Health Surveillance
ramonrcps19@gmail.com

Human T-cell lymphotropic virus type I (HTLV-I) belongs to the family of retroviruses. Enveloped virus has approximately 80-100 nm in diameter. The Env protein presents a high variability, being one of the main components that constitutes the viral particle, being itself responsible for encoding surface and transmembrane glycoproteins. This protein do not posses a tridimensional structure defined. Objectives: To elucidate the three-dimensional model of the Env protein of a HTLV-1 virus. Methods: The env gene of HTLV-1 reference sequence (NC_001436) was translated and the template search was performed using LOMETS in the PDB library. Were retrieved 7 templates (5a9q, 4n21, 3jd8, 4g2k, 5yfp, 6bp2, 517d). The modeling of the Env protein was performed with the Web Server I-TASSER with threading methodology which choose the best alignments measured by Z-score to construct the most confident model. Were generated 5 models that which were validated using software Procheck. Results: The three-dimensional modeling showed good stereochemistry and geometry quality residue-residue globally, with 97.9% of residues in allowed regions. Conclusion: The tridimensional model shows a globular conformation and presenting a stereochemical quality exceeding 97%, may be used to further study drug development inhibitors for HTLV-1.

OBTAINING RECOMBINANT PEPTIDES BY THE PHAGE DISPLAY TECHNIQUE FOR APPLICATION IN THE DIAGNOSIS OF HUMAN T-CELL LYMPHOTROPIC VIRUS INFECTION (HTLV-1).

Siravenha, L.Q.; da Silva, A.N.M.R.; de Freitas, L.S.; de Sousa, R.L.; Queiroz, M.A.F.; Vallinoto, A.C.R.; Goulart Filho, L.R.; Ishak, R.; Machado, L.F.A.

Universidade Federal do Pará.
lsiravenha@gmail.com

The nowadays enzyme immuneassays for HTLV-1 are susceptible to positive or negative false results due to its diversity and the possibility of crossed reactions with other pathological agents, being necessary the discovery of new target peptides. Therefore, the present study had as objective to identify mimetic peptides to the HTLV-1 antigens using the Phage Display technique that were immunoreactive and that may be used in new nanobiotechnological platforms as diagnosis kits. After the biopanning 42 clones were selected according to its reactivity and sequenced. Four viable clones that correspond to the envelope region (gp46), protease, Tax and Rex were obtained. The clones A6, A8, B6 and D7 were submitted to the Phage-Elisa with individual sera of patients bearers of HTLV-1 and control to evaluate the sensibility and specificity. The mimetic peptide B6 was the one that showed the best antigenic potential, with sensibility and specificity of 77.27% ($p < 0.0001$), AUC equal to 0.83 and positive likelihood ratio of 3.4 and may be the candidadte of marker for serological diagnosis of HTLV-1. The clones selected also presented similarity to the HTLV-1's proteins deposited in the GenBank.

OCCURRENCE OF LATE SEROCONVERSION OF INFECTION BY HUMAN T-LYMPHOTROPIC VIRUS (HTLV) IN EX-DONORS OF BLOOD OF ENDEMIC AREA OF THE BRAZILIAN AMAZON.

Borges, M.S.; dos Reis, M.N.L.; Albuquerque, R.S.; de Sousa, M.S.

Universidade Federal do Pará (UFPA).
marizaborges90@hotmail.com

Introduction: Human T-lymphotropic virus (HTLV) is a pathogen belonging to the retrovirus family, which deserves attention due to being associated with serious diseases such as adult T-cell leukemia / lymphoma (LLTA) and HTLV-associated myelopathy paraparesis (HAM / TSP), among others. Seroprevalence rates differ according to geographic area, sociodemographic composition and individual risk behaviors. Pará is the third most prevalent Brazilian state for HTLV infection in blood donors. The metropolitan area of Belém is endemic for this infection (2%), with strong evidence of intrafamily dissemination, both by sexual transmission and by the vertical route. Investigating the occurrence of vertical transmission of HTLV infection in former blood donors is important in identifying and studying cases of late seroconversion. This study aimed to describe the occurrence of possible cases of late seroconversion of HTLV infection in former blood donors in an area endemic to the Brazilian Amazon. Methodology: This is a retrospective study based on data collected by a federal public health teaching unit located in the city of Belém, Pará, Brazil. The study population was composed of blood donors, identified with anti-HTLV-1 / HTLV-2 antibodies, and referred to the teaching unit from January 2008 to April 2018. Results: The university unit attended 747 cases with a mean age of 40 years, of which 52.1% were men, identified by blood bank with anti-HTLV-1 / HTLV-2 antibodies. The presence of the provirus was confirmed in 457 cases and from these it was possible to investigate 52 mothers. HTLV infection was confirmed in 20 (38.4%) mothers, 16 (80%) with HTLV-1 and 4 with HTLV-2. Of these 20 cases that had their mothers confirmed with the infection, 16 (80%) were first-time donors and four (20%) reported being long-term donors. Conclusion: The identification of possible late seroconversion of HTLV infection in long-term blood donors suggests the need for better investigation of these cases, in order to improve the screening of these cases in hemoglobins to prevent transmission of this infection by transfusion of contaminated blood products.

PHYLODYNAMICS ANALYSIS OF THE ENV GENE FROM PTLV.

Ramos, S.A.A.; Gomes, G.P.; dos Santos, R.C.P.; Coelho, R.C.C.; Mendes, W.R.B.; Santos, M.E.S.; de Sousa, M.S.; Nobre, A.F.S.; Sousa Júnior, E.C.

Universidade da Amazônia – UNAMA.
sraugusto47@gmail.com

The Human T-lymphotropic Virus belongs to Retroviridae family, Deltaretrovirus genus. The members that infects human are known as HTLVs and the members that infects Old World Primates are called STLVs (Simian T-lymphotropic Virus), together are called PTLVs (Primate T-lymphotropic Virus). The ENV gene is responsible for coding the GP21/46 proteins that interacts with host proteins. The aim of this study was to describe the evolution of the ENV gene by Molecular Clock. Methods: Were retrieved 104 complete ENV sequences comprising all HTLV and STLV serotypes collected between 2004-2016. The Molecular clock was performed by the software BEASTv.1.8 with Yule as coalescent model in a strict Molecular Clock. Results: The evolutionary rate was 2.9×10^{-7} s/s/y. The PTLV-tMRCA calculated was: 30,010, 154,797, 150,300 and 24,000 years ago for PTLV-1, PTLV-2, PTLV-3 and PTLV-4, respectively. The PTLV-1 clade show two HTLV-1 introductions in 9,135 (6,419 – 11,769, 95% HPD) and 7,085 (5,423 – 8,765, 95% HPD) years ago. Conclusion: the first introduction give origin to the Melanesia genotype and the second introduction to all others circulating genotypes today. These results show that PTLV-1 diverged two times in the past and describe the genetic evolution and specialization of this pathogen in the human and non-human primates

PHYSICAL AND PSYCHOSOCIAL REPERCUSSIONS PRESENTED BY HTLV SEROPOSITIVE PATIENTS.

Dantas, J.B.; Franco, P.S.; Sequeira, C.G.; Neder, P.R.B.

Universidade do Estado do Pará.
paulasilvafranco@hotmail.com

An estimated of 2.5 million people are infected with Human T-Cell Virus (HTLV) in Brazil. Most cases are asymptomatic, although hematological or inflammatory-degenerative manifestations may occur. As pathologies of high morbidity, patients have the tendency to present higher levels of anxiety. The objective of the study was to correlate the physical and psychosocial changes manifested by HTLV seropositives patients. This is a cross-sectional, observational and descriptive study. The data was collected between September 2017 and April 2018, including seropositive HTLV patients that attended the HTLV Clinic of Tropical Medicine Nucleus of the Federal University of Pará. The instruments used to collect data were: interview scripts, Beck Anxiety Inventories (BAI) and chart analysis protocols. Thirty-Three patients participated in the study: 81.8% was women, 42.4% was between 40-55 years old and 75.8% was from Belém-PA. Around 45% presented moderate to severe anxiety and 72,7% presented clinical manifestations. Patients with further physical alterations had an elevated level of anxiety ($p = 0.0220$). Accordingly, women between age of 40-55 years old with clinical symptoms and high prevalence of moderate to severe anxiety, exhibit a positive association between clinical manifestations and level of anxiety, demonstrating the importance of the psychological component in HTLV infection.

PREVALENCE OF HUMAN T-LYMPHOTROPIC VIRUS INFECTION IN A MILITARY HOSPITAL OF BELÉM, PARÁ, BRAZIL.

de Melo, T.G.; de la-Roque, D.L.; Almeida, G.B.S.; dos Santos, C.C.M.; Borges, M.S.; de Alcântara, V.G.; Guimarães, V.S.; Covre, L.S.C.; Pereira, C.C.C.; de Sousa, M.S.

Universidade Federal do Pará.
talita.go.me@hotmail.com

Introduction: The human T-lymphotropic virus (HTLV) has widespread unfamiliarity of the population. Transmission occurs through sexual contact, blood route and, vertical pathway. Approximately, 90% of those infected remain asymptomatic. There may be muscle, neurological, joint and cancer complications. There is no specific treatment and the prognosis depend on the evolution of the case. The military is on constant missions and also work in possible endemic areas, thereby, has become a public vulnerable to infection. **Objective:** In this study, we investigated the prevalence of HTLV infection in a military hospital in Belém, Pará. **Method:** The cross-sectional descriptive-analytical model was used and, serological screening of anti-HTLV antibodies was carried out, followed by a molecular analysis of the provirus and identification of viral type. **Results:** 331 subjects (67%) accepted to participate in the study. Of the 331 cases investigated, 54.38% were women and 45.62% were men. The age range varied from 18 to 87 years, 73.1% came from the state itself, 94.3% live in the metropolis, 46.5% are military, 62.8% are brown, 83.4% are from the health sector, 52.6% are married or live together and 46.2% do not have a partner. A prevalence of 0.60% (2/331) of the infection was obtained in the study population. Of those infected, one man was a 55-year-old military man with HTLV-1 and a pensioner woman, 60 years old with HTLV-2. Both browns, without spouses. The family research was not possible. **Conclusion:** Screening for HTLV in the military and their families showed a low frequency of infection in this demand.

RELIABILITY OF DIFFERENTIALS OF THE DGI, BESTEST, BBS AND TUG BALANCE IN HAM/TSP INDIVIDUALS.

de Sousa, M.C.; Nunes, R.F.R.; Leme, A.P.C.B.P.; Souza, C.R.J.; Lisboa, C.K.R.; Nascimento, D.J.; da Fonseca, E.P.; Sá, K.N.; Pinto, E.B.

Católica University of Salvador, Bahiana School of Medicine
mayrasousa@bahiana.edu.br

Although HAM / TSP is a clinical condition that can result in alterations in functional performance, there are still no validated scales for this population with greater data reliability. The goal was to verify the inter-rater reliability of the Dynamic Gait Index (DGI), Balance Evaluation Systems Test of dynamic balance (BestTest), Berg Balance Scale (EEB) and Timed up and Go (TUG) scales. Methods: Individuals with HAM / TSP, both sex, age between 18 and 64 years and independent gait, were evaluated by two trained examiners, in the same shift, with a time interval between evaluations. The project was approved by the Research Ethics Committee with CAAE 77594617.0.0000.5628. A statistically significant difference was considered at $P < 0.05$. Results: The inter-rater reliability of the scales was excellent for GI (ICC=0.755 $P=0.002$), BestTest (ICC=0.772 $P=0.002$), and BSE (ICC=0.907 $P < 0.001$) and satisfactory for TUG (ICC=0.658 $P=0.012$). And the level of agreement was considerable for BSE (kappa=0.792 $P=0.024$), almost perfect for DGI (kappa=1,000 $P=0.018$) and TUG (kappa=1,000 $P=0.018$). Conclusion: It was verified that EEB, DGI, BestTest and TUG can be used with good reliability for this population.

RESEARCH OF HUMAN T-LYMPHOTROPIC VIRUS IN STUDENTS OF A PUBLIC UNIVERSITY OF THE METROPOLITAN REGION OF BELÉM, PARÁ.

Pereira, C.C.C.; de La-Roque, D.G.L.; Silva, I.C.; Almeida, D.S.; Covre, L.S.C.; Vieira, R.C.; da Costa, C.A.; de Sousa, M.S.

Universidade Federal do Pará/Núcleo de Medicina Tropical.
cassiaccpereira@hotmail.com

HTLV-1 sexual transmission is more effective from man to woman. Studies have detected the viral genome in infected semen and vaginal secretion. College students are more exposed to infectious and sexually transmitted diseases. This study aimed to detect previously infected lymphocytes in endocervical samples of university students, simultaneously to the search in the blood (including men). Methods: Searches for Anti-HTLV antibody (ELISA) and viral genome (PCR) tests were performed on peripheral blood and vaginal secretion (PCR only). Results: A total of 326 young people (55 men and 271 women) was investigated. Where they were investigated: 116 only in blood, 105 only in secretion and 102 in blood and secretion. There were no positive cases for the HTLV investigation. We also found: 10 women positive for *Chlamydia trachomatis* and 35 for HPV in secretion, and 2 for syphilis. The epidemiological profile of students attended was also described. Conclusion: Condom use is still considered low. It was not possible to perform early detection (prior to HTLV-reactive serology) from vaginal secretion. Factor that may be associated with low amount of infected lymphocytes in the endocervical region, constant cell renewal of the uterus due to menstruation and slow progression of the disease.

SEXUAL RESPONSE AND AFFECTIVE BONDING IN WOMEN WITH HTLV-1.

Bendelack, R.M.; Lemos, C.I.L.; Câmara, C.N.S.; de Sousa, R.C.G.

Universidade Federal do Pará.
rayanne_lisboa@hotmail.com

In recent years, sexually transmitted infections (STIs) again have increased in incidence in different countries, including Brazil. STIs can lead to several complications for the infected person in different domains of their life. Among these STIs, human T-cell lymphotropic virus type 1 (HTLV) infection stand out, since they can lead to physiological alterations, causing physical limitations, behavioral changes and social impact. Objectives: Investigate the sexual response and affective bonding in women with and without HTLV-1. Method: The study was conducted in the city of Belém-Pará in which participated 64 women, allocated in 4 groups, 19 seropositive women for HTLV-1 (REP+) and 20 women without the virus (REP-), both in the reproductive period and 10 seropositive woman of HTLV-1 (MEN+) and 15 seronegative women of HTLV-1 (MEN-), both in postmenopause. Were used Socioeconomic questionnaire, Female Sexual Function Index and Love Scale. Results: women in the reproductive phase with HTLV-1 presented differences in sexual response, arousal and desire as compared to women in the reproductive phase without the virus and low affective bonds were correlated to lower sexual satisfaction and arousal in postmenopausal seropositive women. Conclusion: There was alterations in sexual response and affective bonds in women with HTLV-1.

SEXUAL RESPONSE IN WOMEN IN THE REPRODUCTIVE PERIOD WITH HTLV-1.

Bendelack, R.M.; Lemos, C.I.L.; Câmara, C.N.S.; de Sousa, R.C.G.

Universidade Federal do Pará.
rayanne_lisboa@hotmail.com

Sexual health is a physical well-being, emotional, mental and social, not configuring only in the absence of disease or sexual dysfunctions, but the interaction of biopsychosocial aspects. HTLV-1 is a debilitating pathogen that has biological properties capable of infecting cells of the human immune system, which may lead to changes in the sexual health of infected women, causing loss of libido, orgasm and dyspareunia, as well as the disruption of affective-sexual relationships. Objectives: Investigate the sexual response in women with HTLV-1 and women without virus. Methods: Participated in the study 39 women, allocated in 2 groups, 19 seropositive women for HTLV-1 (REP+) and 20 women without the virus (REP-), both in the reproductive period. Were used Sociodemographic Questionnaire and Female Sexual Function Index (FSFI). Results: It was verified that the REP + group showed differences in the total sexual response score, desire and sexual arousal compared to REP-. Conclusion: HTLV-1 infection, possibly, causes negative impact of sexual response in women in the reproductive phase infected by this virus, beyond a decline of desire and excitement.

TEN YEARS OF INVESTIGATION OF INTRAFAMILIARY TRANSMISSION OF HUMAN T-LYMPHOTROPIC VIRUS 1 (HTLV-1) IN A ENDEMIC REGION OF THE AMAZON.

de Araújo, M.W.L.; Dantas, A.S.F.; da Costa, C.A.; de La-Roque, D.G.L.; Silva, I.C.; Oliveira, J.F.G.; Lopes, K.B.; Bastos, L.S.S.; Covre, L.S.C.; Borges, M.S.; Soares, M.N.; de Sousa, M.S.

Universidade Federal do Pará.
marcosw09@outlook.com

HTLV, Human T-Lymphotropic Virus was the first retrovirus discovered in humans. Transmission can occur through sexual intercourse, by those who have already received transfusion and / or by those who share contaminated needles or syringes, through breastfeeding and in the intrauterine period or after childbirth. This study aims to describe the results of a ten-year study of intrafamilial transmission of HTLV-1 in an endemic region of the Brazilian Amazon. Methods: An outpatient, descriptive and analytical observational study, developed prospectively by monitoring the HTLV-1 family cohorts between 2008 and 2017. Results: Of the 160 families investigated, 78 (49.0%) had at least two infected members, not ruling out the possibility that in the remaining 82 families (51.0%) there were other infected members, since there is no complete family membership. In the search for sexual transmissions, we identified 94 voluntary study couples, of whom 41 (43.7%) had (both spouses) the viral infection. Regarding vertical transmission, we researched 179 pairs [mother-child], of whom, in 43 (24.0%), there was a probable transmission. Conclusion: Intrafamilial transmission of HTLV-1 is essential for the silent spread of the virus in the region, in which sexual transmission is highlighted as the most important.

THE IMPACTS OF PHYSIOTHERAPY REHABILITATION IN SPASTIC TROPICAL PARAPARESIS PATIENTS: A SISTEMATIC REVIEW

de Souza, L.B.R.; do Nascimento, D.C.S.; de Andrade, A.A.S.; Pinto, D.S.

Universidade Federal do Pará
brynneleonard@hotmail.com

Introduction: Human T-Lymphotropic Virus 1 (HTLV-1) is a virus which has a wide group of symptoms. Infected population is subdivided in assymptomatic patients, and symptomatic patients, in this last group, symptoms indicates casually Lymphoma or Tropical Spastic Paraparesis (TSP). In TSP, it's observed a progressive loss of movement and sensibility, but it's believed physiotherapy rehabilitation strategies can reduce progression of TSP. Objective: Verify the impacts of physiotherapy's rehabilitation in Spastic Tropical Paraparesis patients. Methods: This work is a systematic review, using the databases: PUBMed, PUBMed Health, PMC, Medline, BVSalud, Scielo, Bireme and Lilacs. The keywords were "HTLV-1 rehabilitation", "HTLV-1 physiotherapy", "HTLV-1 treatment", "Tropical Spastic Paraparesis rehabilitation"e "Tropical Spastic Paraparesis physiotherapy". It was included exclusively articles written in portuguese or english, published posteriorly to 2012 and which followed an experimental model, applying an intervention method over symptoms resulting of TSP. It was started with 92, but it was finished with 10. Results: All the physiotherapy's rehabilitations strategies were effective to reduce the pain, loss of motricity, functionality and emotional damage in HTLV'1 patients symptomatic positives to TSP. Conclusion: physiotherapy's rehabilitation strategies are efficient to control TSP symptoms.

THE NURSES' KNOWLEDGE TOWARDS THE DIAGNOSIS AND TREATMENT OF HUMAN T- CELL

Carvalho, E.L.L.D.; de Souza, N.S.; de Moraes, M.R.

Universidade da Amazônia
liraelanel@gmail.com

Introduction: T-lymphocyte virus (HTLV) infects defense T cells, especially LT-TCD4, being associated with severe and poorly understood pathologies. HTLV infection is endemic in the state of Pará - Brasil, therefore, it is indispensable for the health professionals to be aware of the virus in order to provide a suitable and humanized assistance. Objectives: To analyze the knowledge of nurses that work in the primary care of the Ananindeua city on the diagnosis and treatment of HTLV-I / II virus. Methods: This was a descriptive, cross-sectional epidemiological study with a quantitative approach, which was carried out collectively, with anonymous and voluntary participation of the nurses. Results: Through the application of a questionnaire, we obtained epidemiological data and checked the specific knowledge about the virus by the nurses that was represented graphically. Conclusion: This work represents the first step to provide concrete data about the nurses' knowledge of HTLV-I / II virus, who work in the primary care of the city of Ananindeua-PA. Bringing up the need to sensitize public health policy managers to invest in training and updating health professionals to ensure a humanized care.

THERAPEUTIC EFFECT OF THE PILATES METHOD ON FUNCTIONAL PERFORMANCE IN PEOPLE WITH HAM/TSP: RANDOMIZED CLINICAL TRIAL

da Conceição, A.C.R.; da Fonseca, E.P.; de Souza, M.C.; Nunes, R.F.R.; Leme, A.P.C.B.P.; Souza, C.R.J.; Lisboa, C.K.R.; Nascimento, D.J.; Pinto, E.B.C.; Sá, K.N.

Universidade Católica de Salvador
adriano.celso@outlook.com

Introduction: Individuals with HAM / TSP have sensory changes, which can affect functional time. The therapeutic indicators, we have the Pilates method (MP), with evidence are insipient for this population. The aim was to verify the therapeutic effect of MP in people with HAM / TSP. **Methods:** This was a clinical trial in which individuals with independent gait were randomly assigned into two groups with HAM / TSP, both sexes, adults, with independent gait. Task-oriented training. Those that were amputation, pregnancy, and other associated neurological disorders were ruled out. Before and after 20 teaching sessions, demographics and resources, balance, functional mobility, gait balance, fatigue, and gait resistance were distributed. The project had just published by CAAE 80389317.8.0000.5628. It made a statistically significant difference $p < 0.05$. **Results:** Eleven patients were selected, 54.54% female, 48.25 years of age and 91% with gaiters. It was not addressed to the separation between the groups in any measure used. However, it is important that all groups achieved improvement in all measures after an intervention. **Conclusion:** MP can be an instrument in the rehabilitation of people with HAM / TSP.

EVALUATION OF ANNEXIN 1 AS A CLINICAL PROGNOSIS BIOMARKER IN HTLV-1 INFECTION

Santana, B.B.; da Silva, R.A.; Valentim, C.Y.U.P.A.; Amoras, E.S.G.; Rodrigues, C.M.; de Sousa, M.S.; Goulart, L.R.; Vallinoto, A.C.R.

Universidade Federal do Pará
Universidade Federal de Uberlândia
biomedicinabarbara@gmail.com

Introduction: HTLV-1 presents lymphocyte tropism. It is associated with a chronic neurodegenerative disease, called HTLV-1 Associated Myelopathy/Tropical Spastic Paraparesis (HAM/TSP). Studies with Annexin A1 (ANXA1) have identified it as a glucocorticoid-induced protein, involved in the synthesis of eicosanoids and phospholipase A2. The present study aimed to investigate the genetic and proteic influence of Annexin A1 and its receptors in patients with HTLV-1 infection. **Methods:** Peripheral blood mononuclear cells from HTLV-positive asymptomatic (PA) and HAM/TSP patients were evaluated for the expression of endogenous ANXA1, FPR1, FPR2 and FPR3 genes by qPCR. The ANXA1 profile in CD4+, CD8+ T cells, granulocytes and monocyte subpopulations was determined. **Results:** The gene expression of ANXA1 was increased and its respective receptors decreased in the PA group when compared to HAM/TSP. In the CD4+ T, CD8+ T lymphocytes, intermediate subpopulations of monocytes and granulocytes the percentage of ANXA1+ was higher in the PA group as compared to the other groups. **Conclusion:** The results obtained showed evidence that ANXA1 may be a potential biomarker of differential prognosis of neurodegenerative disease.

CHIMERIC PROTEIN LVBA-recHTLV-1/2 SHOWED GREAT SENSITIVITY IN INDIRECT ELISA IN HOUSE USING SERA FROM PARÁ AND MARANHÃO HTLV-1/2 COHORTS

Franco, G.M.; Rocha, A.S.; Martins, M.L.; Romanelli, L.C.; Ishak, R.; Vallinoto, A.C.R.; Bomfim, M,R,Q.; da Fonseca, F.G.; Barbosa-Stancioli, E.F.

Universidade Federal de Minas Gerais
Universidade Federal do Pará
gabymelofranco@yahoo.com.br

The Human T-lymphotropic virus (HTLV-1/2) can induce neurological and neoplastic diseases and have high prevalence in Brazil. The development of tests based on national biotechnology for screening blood products is essential to ensure the implementation and maintenance of public health programs, bringing the perspective of reducing costs, minimizing viral transmission and improving epidemiological data. Due to the mandatory screening in blood centers and the need to extend HTLV-1/2 screening to other groups, this project aimed the evaluation of the chimeric protein LVBA-recHTLV-1/2 as antigen [Env, Gag and Tax epitopes of HTLV-1 and HTLV-2] in an indirect ELISA in house using biological samples from North and Northeast Brazilian States, Pará and Maranhão. Double-blinded analysis were carried out in 301 sera: 28 HTLV-1+, 7 HTLV-2+, 49 HTLV-/HIV+ and 27 HTLV- from Pará, 3 HTLV-1+, 2 HTLV-/HIV+, 3 HTLV-/HBV+ and 182 HTLV- from Maranhão cohort. Results showed 100% sensitivity and specificity higher than 75% in both cohorts. Given the prevalence of HTLV in Maranhão is 0,15% and 0,9% in Pará, the accuracy of the test was higher than 75% in both cohorts with efficiency of 100%. Data shown that LVBA-recHTLV-1/2 has potential to be used in commercial diagnostic tests for HTLV in Brazil.

RELIABILITY OF OABSS, AGACHAN and WEXNER SCALES IN HAM/TSP INDIVIDUALS

Nunes, R.F.R.; Fonseca, E.P.; Leme, A.P.C.B.P.; Souza, C.R.J.; Sousa, M.C.M.; Menezes, N.S.

Universidade Católica de Salvador
reebecaa.nunes@hotmail.com

Introduction: HAM/TSP consists of an clinical inflammatory condition that results in a set of progressive and disabling signs and symptoms, such as sphincter disorders. However, there are still no validated scales for this population with greater data reliability. The objective was to verify the inter-examiner reliability of the OABSS, Agachan and Wexner scales. Methods: Individuals with HAM/TSP, both sex, age between 18 and 64 years and independent gait, were evaluated by two trained examiners, in the same shift, with a time interval between evaluations. The project was approved by the Research Ethics Committee with CAAE 77594617.0.0000.5628. A statistically significant difference was considered at $p < 0.05$. Results: The inter-examiner reliability of the scales was excellent for Agachan (ICC = 0.772, P = 0.002), for Wexner (ICC = 0.918, P = 0.001) and OABSS (ICC = 0.797, P = 0.001). And the level of agreement was considerable for Agachan (KAPPA = 0.633, P < 0.001) and Wexner (KAPPA = 0.718, P = 0.003). Conclusion: It was verified that the OABSS, Agachan and Wexner scales can be used, with good reliability, to evaluate this population.

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