



**The diagnosis of
human T lymphotropic
virus (HTLV)
and strategies
to expand HTLV
screening
in the context of
maternal and child
health**

Meeting Report (virtual),
7 July 2023

PAHO



Pan American
Health
Organization



World Health
Organization
REGIONAL OFFICE FOR THE
Americas

The diagnosis of human T lymphotropic virus (HTLV) and strategies to expand HTLV screening in the context of maternal and child health. Meeting Report (virtual), 7 July 2023

PAHO/CDE/HT/23-0014

© Pan American Health Organization, 2023

Some rights reserved. This work is available under the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 IGO license (CC BY-NC-SA 3.0 IGO).

Under the terms of this license, this work may be copied, redistributed, and adapted for non-commercial purposes, provided the new work is issued using the same or equivalent Creative Commons license and it is appropriately cited. In any use of this work, there should be no suggestion that the Pan American Health Organization (PAHO) endorses any specific organization, product, or service. Use of the PAHO logo is not permitted.

All reasonable precautions have been taken by PAHO to verify the information contained in this publication. However, the published material is being distributed without warranty of any kind, either expressed or implied. The responsibility for the interpretation and use of the material lies with the reader. In no event shall PAHO be liable for damages arising from its use.

**The diagnosis of human
T lymphotropic virus
(HTLV)
and strategies to expand
HTLV screening
in the context of maternal
and child health**

**Meeting Report (virtual),
7 July 2023**

Washington, D.C., 2023

PAHO



**Pan American
Health
Organization**



**World Health
Organization**
REGIONAL OFFICE FOR THE
Americas

CONTENTS

Abbreviations and acronyms	vi
Summary	1
Rationale	2
Purpose of the meeting	2
Opening ceremony	3
HTLV diagnosis	3
Diagnosis in pregnant women: State of the art and perspectives	3
Diagnosis in blood banks: Overview and strategies to improve service and surveillance in the Americas	4
National experiences and perspectives	6
Chile: Current practices for blood donor screening and perspectives on antenatal screening	6
Brazil: Strategies to expand access to HTLV-1 diagnosis in Brazil	7
Saint Lucia: HTLV-1 screening in the antenatal care and leveraging the EMTCT Plus Initiative	7
Colombia: HTLV-1 diagnosis in pediatric patients and follow-up of exposed infants	7
Argentina: Improving HTLV-1 diagnostics through international collaboration	7



Closing Remarks	8
Conclusion	8
List of figures, tables and boxes	
Figure 1. Criteria to accept or defer blood donors, according to HTLV-1 status and risk of infection	9
Table 1. Clinical manifestation of HTLV-1 infection in pediatric patients	9
Box 1. Take home messages	10
References	12



ABBREVIATIONS AND ACRONYMS

ATLL	adult T-cell leukemia lymphoma
EMTCT	elimination of mother-to-child transmission
ELISA	enzyme linked immunoassay
HTLV	human T lymphotropic virus
HTLV-1	human T lymphotropic virus type 1
HTLV-1/2	HTLV type 1 and/or type 2
HAM	HTLV-1 associated myelopathy
LIA	line immunoassay
PAHO	Pan American Health Organization
PCR	polymerase chain reaction
STI	sexually transmitted infection
UK	United Kingdom
WB	western blot
WHO	World Health Organization

SUMMARY

This workshop aimed to discuss the diagnosis of Human T lymphotropic virus (HTLV) infection with HTLV experts, representatives of Member States, and civil society. Diagnosis of HTLV-1 is based on an algorithm comprising screening and confirmatory tests. The algorithm varies in different countries, and international guidance on HTLV-1 diagnostics would be beneficial. Coverage of blood donation screening is high in the Region of the Americas but still incipient in antenatal settings. Increased interest in HTLV-1 antenatal screening has been observed in the Region, and Chile, Brazil, Saint Lucia, and Colombia shared their experience during the workshop. Good practices included a program to prevent HTLV-1 mother-to-child transmission integrated with the Elimination of Mother to Child Transmission (EMTCT) Plus initiative in Saint Lucia; strong collaboration between civil society, HTLV-1 experts, and policymakers in Brazil; initiatives to increase awareness about HTLV-1 in the Region; and the construction of HTLV clinical guidelines by different countries in the Americas. Priorities were identified, including increasing awareness about HTLV, developing guidelines and support training for health care professionals, strengthening collaboration between countries, and promoting the inclusion of HTLV into elimination programs.

RATIONALE

The Pan American Health Organization (PAHO) and its Member States recognize the human T lymphotropic virus type 1 (HTLV-1) as a matter of concern in the Region. In recent years, PAHO has been engaging with different stakeholders, including HTLV-1 specialists, health managers, and people living with HTLV-1 to define priorities and to delineate effective strategies to tackle this neglected infection. One of the priorities is the prevention of HTLV-1 mother-to-child transmission. However, to be able to prevent vertical transmission, pregnant women living with HTLV-1 must be aware of their status. The coverage of HTLV-1 screening of blood donors is high in the region, but antenatal screening is still limited. Countries still face barriers to implement diagnostic tests for HTLV. There are no international guidelines for HTLV-1 diagnostics, and national guidance may vary between countries. In this context, PAHO and the HTLV Channel conducted a workshop to discuss the diagnosis of HTLV-1 infection, particularly in the context of maternal and child health.

The recordings of the workshop are available at PAHO TV on YouTube in the original audio; Portuguese, English, and Spanish.

The organization of the webinar and the preparation and publication of this meeting report was funded by the Government of Canada.

PURPOSE OF THE MEETING

Specific objectives of this workshop included:

- To discuss the laboratory diagnosis of HTLV-1 infection, including diagnostic algorithms and performance of laboratory assays;
- To share experiences of different Member of States regarding HTLV-1 diagnosis, including current practices, challenges, and perspectives;
- To promote discussion about the laboratory follow-up of HTLV-1-exposed infants;
- To delineate strategies to reduce the costs of HTLV-1 diagnosis and to overcome current barriers.

OPENING REMARKS

Dr. Leandro Sereno opened the webinar by pointing to the two Workshops (1, 2) that preceded this meeting and the rationale behind the workshop. Dr. Massimo Ghidinelli addressed the importance of maintaining interest in HTLV-1, particularly in the post-pandemic era. He identified a favorable scenario for this discussion in the Americas. Under the leadership of Dr. Jarbas Barbosa, PAHO has strengthened its focus on transmissible diseases, with particular interest on the elimination of infectious diseases. PAHO is working with a portfolio of more than 30 candidates for elimination, and he is keen to include HTLV-1 in this list in the near future.

Dr. Tatiane Assone acknowledged PAHO's partnership and support. She pointed out that diagnosis of HTLV-1 infection is a crucial step in the response to HTLV-1 and asked the community to expand discussions on the diagnosis of pediatric patients. According to Dr. Assone, these workshops are essential to ensure that HTLV is included in the agenda and for the allocation of resources for the implementation of policies. She stressed funding for research, including on strategies to follow up on exposed infants, as a priority.

Ms. Angela Maria Feitosa shared her lived experience as a woman living with HTLV-1 and the difficulties of being misdiagnosed when her first symptoms of HTLV-1 associated myelopathy (HAM) started at the age of 33, following vertical transmission. According to Ms. Feitosa, the number of people living with HTLV is high, but the lack of testing leads to an underestimation of the real burden of HTLV. She highlighted the need for multidisciplinary care for the follow-up of patients and the challenges faced by those who have a progressive disease. There is a need to increase awareness about HTLV and to empower those living with this virus. Ms. Feitosa has been working to increase awareness about HTLV in her region and has been engaging successfully with policymakers and politicians. Her main priority is the implementation of HTLV antenatal screening and confirmatory testing, as has been done for HIV, syphilis, and hepatitis. She urged health care professionals and Member States to test pregnant women and exposed infants.

HTLV DIAGNOSIS

DIAGNOSIS IN PREGNANT WOMEN: CURRENT STATUS AND PERSPECTIVES

Professor Graham Taylor (Imperial College London) started his presentation by addressing the rationale for antenatal screening: the opportunity to inform those women living with HTLV of strategies to prevent HTLV transmission to their infants and ultimately to prevent HTLV-associated diseases, especially adult T-cell leukemia/lymphoma (ATLL), which mainly affects those infected during infancy. He emphasized the efficiency of diagnostic tests in pregnancy by showing data obtained in the United Kingdom (UK) cohort (3), confirming that pregnancy does not negatively affect the diagnosis of HTLV. Taylor pointed out that information on assays' performance reported by the World Health Organization (WHO) in the HTLV technical report (4) comes from a compilation of assays and studies over 30 years, underestimating the performance of the assays that are in use. The currently commercially available third and fourth generation screening assays are highly sensitive (100%) and specific (99.8–99.9%). It is also possible to refine the interpretation of the screening assays by adjusting the assay's cutoff for positivity. As an example, he pointed that in the UK, samples with reactivity between 1–4 in Abbott Architect are never confirmed positive whilst nearly all samples with a sample's signal to cutoff ratio above 20 are confirmed as HTLV. This may help to reduce the need for confirmatory test.

Screening tests will detect the presence of antibodies to HTLV type 1 and/or type 2 (HTLV-1/2). Confirmation of infection and viral typing are required. Western blot (WB) is the traditional method to confirm HTLV-1/2 infection, and although there are issues related to the cost, it has a good overall performance. The line immunoassay (LIA) is relatively simple with lower number of bands than WB, and this may reduce non-specific reactivity.

Taylor also presented diagnostic algorithms, including an algorithm from HTLV European Research Network (HERN), Sweden, Japan, Brazil, and Chile (5–8). He suggested that repeated screening test are no longer required due to the high specificity and sensitivity of screening assays. Reactive samples in screening tests should be submitted to confirmation. Pooling samples saves on reagent costs and is suitable for large scale testing. This strategy was used by the National Health Service Blood Transfusion in the UK to screen blood donations from 2002 to 2015. Pooling samples may also reduce non-specific reactivity.

The polymerase chain reaction (PCR) assay is an alternative that may be used as a confirmatory test. It can be developed in-house, reducing costs. Some patients with very low proviral load may have a false negative result, but Taylor pointed that these individuals are unlikely to transmit the virus because of their very low load. He identified the need for an additional sample as the major drawback of PCR testing as it may delay results and some patients may be lost during follow-up. This concern is of particular interest in patients who present late at pregnancy. HTLV-1 point of care tests are in the pipeline (9), and PCR assays are now commercially available (although not widely spread). This access will facilitate diagnosis.

Quality control is a challenge, and international collaboration may be useful to ensure the quality of the diagnosis. There is a need for international guidance for HTLV-1 diagnosis, and simple algorithms are preferred. Another challenge is to improve counselling and linkage to care to help mothers to make informed decisions about strategies to prevent transmission. Targeted screening may be considered in some scenarios to reduce costs, and the option to test pregnant women considered at high risk of infection is under consideration in the UK.

When asked about the challenges and strategies to overcome barriers to implement antenatal screening, he highlighted that the UK has a well-established referral system, but the challenge is to identify those who are living with the virus. He identified two major barriers that are also common in most countries: limited resources and lack of knowledge about HTLV. In this context cost-benefit analysis is very important. To overcome the lack of knowledge, UK HTLV experts are producing relatively simple guidance for health care professionals, including information on how to test, how to manage patients with positive results, and where to refer them for follow-up.

Box 1. Take home messages

- There are highly sensitive and specific tests to diagnose HTLV infection in pregnant women;
- Antenatal screening programmes already exists for other bloodborne infections;
- Pregnant women have the right to know their serostatus to be able to make informed decisions on prevention strategies;
- Strategies to reduce costs are available;
- Barriers to overcome relate primarily to knowledge and understanding about the consequences of HTLV-1 infection.

HTLV SCREENING IN BLOOD BANKS: OVERVIEW AND STRATEGIES TO IMPROVE SERVICE AND SURVEILLANCE IN THE AMERICAS

Dr. Mauricio Beltran Duran (PAHO) provided attendants with an overview of the current status of HTLV screening in blood banks in the Americas, which aims to guarantee the safety of the blood products. HTLV is one of the recommended targets for screening according to local epidemiology. The selection of voluntary blood donors who are considered low risk is the first step to ensuring the quality of the blood product. However, some donors may fail to answer properly the health questionnaire, and some may have subclinical and asymptomatic infection. Therefore, screening is important. Other processes, such as leucodepletion, may be used to reduce the risk of transmission of bloodborne pathogens. Leucodepletion significantly reduces the risk of transmitting pathogens.

Figure 1. Criteria to accept or defer blood donors, according to HTLV-1 status and risk of infection.

Accept	Defer temporarily	Defer permanently
<ul style="list-style-type: none"> • Household members of a person living with HTLV-1/2 • Potential donors whose mother or maternal grandmother has or had HTLV-1/2 and the donor is negative 	<ul style="list-style-type: none"> • Former sexual contacts of individuals with HTLV-1/2 • Current sexual contacts of individuals with HTLV-1/2 	<ul style="list-style-type: none"> • Individuals living with HTLV-1/2 • Potential donors whose mother or maternal grandmother has/had HTLV-1/2, if blood screening is not available

Screening tests need to be highly sensitive to be able to detect low levels of antibodies, antigens, or nucleic acid. High specificity is important to avoid discarding blood donations due to false positive results. Dr. Duran pointed the criteria to accept or defer blood donors, according to their HTLV-1 serostatus and their risk of infection (Figure 1). He commented that HTLV screening of blood donation is implemented in 21 of the 36 countries and territories that report to PAHO, and prevalence is usually low. He highlighted that the donor population is considered low-risk and prevalence in general population is higher. Some countries perform confirmatory tests for HTLV, and each country has their own diagnostic algorithm. Arguments used to underpin the importance of notification of donors with reactive tests include results are important for donors' lives; it will prevent new donations; ethical duty to inform about a possible disease (acute or chronic); prevent secondary transmissions (sexual and vertical transmission), explain about transmission routes and why the donor was excluded from blood donation; refer to care (if applicable); surveillance; contact tracing (if needed).

At the end of his presentation, a question was raised about the current situation of countries in the Americas regarding counselling and linkage to care and if there is capacity to expand this testing system to include antenatal screening. Dr. Duran indicated that the situation in the Region is very heterogeneous and there is a need to improve the link between hemovigilance and surveillance and epidemiological data. In his opinion, countries need to strengthen the available system to optimize the service that is already implemented.

NATIONAL EXPERIENCES AND PERSPECTIVES

Moderator: Carolina Rosadas (HTLV Channel, Imperial College London)

CHILE: CURRENT PRACTICES FOR BLOOD DONOR SCREENING AND PERSPECTIVES ON ANTENATAL SCREENING

Dr. Jorge Valdebenito Pino, from Chile's Ministry of Health, presented on the current status of Chile. In 2009 Chile published a national policy for blood donations. In 2021, an update included some relevant actions, such as health questionnaires for all potential donors and national HTLV screening of all blood donations. A central laboratory performs HTLV confirmatory test for samples with reactivity in the screening test; less than half of samples that are positive during screening are confirmed. Chile implements a good practice of compiling information on the number of donors who test positive for HTLV in both screening and confirmatory tests. Dr. Pino demonstrated that HTLV-1/2 is present in all Chilean territory, but infection is concentrated in the north. This was assessed using data from blood donation screening, highlighting the usefulness of such information. Data from the central laboratory confirmed ongoing vertical transmission, and Chile is preparing a national guidance on prevention of HTLV vertical transmission. This guidance will include provision of complimentary infant formula and cabergoline to reduce the risk of HTLV transmission, like what is done for mothers living with HIV. This guidance will also include counselling to avoid secondary transmission (not limited to vertical transmission) and contact tracing. Antenatal screening will be offered regionally in local hospitals to facilitate access and improve coverage. A pilot study of antenatal screening in a high prevalence area is ongoing.

Despite recent advances and promising perspectives, some barriers remain. These include the absence of compulsory notification; limited prevalence data, which is restricted to blood donors; lack of cost-effectiveness studies on antenatal screening; and limited funding. To

conclude, Dr. Pino listed actions needed. From a national perspective, there is a need to strengthen the surveillance and notification systems, to gather more information on clinical outcomes to guide public policies, and to improve training of health care professionals. As for the support needed from PAHO, he recommended the recognition of HTLV as a public health concern in the Region and stressed that advocacy at high levels in the ministries of health of Member States is welcomed. PAHO may support countries to develop their national programs. Finally, he suggested that inclusion of HTLV in regional strategies and activities (such as EMTCT Plus) would be beneficial.

BRAZIL: STRATEGIES TO EXPAND ACCESS TO HTLV-1 DIAGNOSIS IN BRAZIL

Professor Angelica Miranda, of Brazil's Ministry of Health, shared the history of Brazil's screening: HTLV screening in blood donations has been done since 1993 and in organ donors and recipients since 2009. However, screening is limited to these specific populations. She mentioned that, after the WHO expert meeting about HTLV in 2019, Brazil's Ministry of Health realized the need to advance their response to this virus. Following that meeting, she developed a study, in collaboration with the scientific society, to better understand the scenario for HTLV. The research identified strengths, weaknesses, opportunities, and threats to the inclusion and expansion of policies to HTLV (10).

Brazil is now working to overcome the threats and weaknesses. The first step to increasing coverage of HTLV testing is to increase awareness about HTLV. The Ministry of Health has been including HTLV in online training courses and clinical protocols for sexually transmitted infections (STIs) and maternal and child health programs. It has also included its HTLV diagnostic algorithm in leaflets to support health care professionals. A drawback is that although Brazil has these algorithms, tests are not offered nationally. It is easier to expand access to testing in the private sector, but to implement it in the public health system is more challenging. Screening and confirmatory test for HTLV are offered for pregnant women in some states and cities only. A similar scenario exists for blood donations: confirmatory testing is restricted to some areas. They have mapped the centers for patient care and observed that they are not equally distributed in the country, and most of them lack government funding.

According to Miranda, testing pregnant women is essential as the Ministry of Health already recommends avoiding breastfeeding and to formula feed exclusively to those women who are living with HTLV. The country provides complimentary formula and cabergoline to stop lactation. However, she pointed out that they must identify those who are infected, which can only be done if testing is offered in the antenatal care. Further, the policy regarding the provision of formula does not consider that other family members may consume the formula, and this factor may impact on the quantity of milk substitute available for the infant. Universal HTLV antenatal screening is under consideration by The National Committee for Health Technology Incorporation (CONITEC)¹. Due to the high number of pregnant women in the country, the cost of testing is very high, but a recent study showed that this policy would be cost-effective and that policymakers should also balance the negative impact in those mothers who transmit the virus to their infants.

Miranda also pointed to the need for more research on HTLV. The development of a low-cost point of care test is one opportunity to increase coverage. Currently, two tests produced by Brazilian researchers are in late-stage validation and are seeking regulatory approval to be offered.

¹ Following the webinar, the CONITEC concluded the evaluation, recommending the incorporation of universal HTLV screening as part of antenatal care services: <https://www.gov.br/conitec/pt-br/assuntos/noticias/2024/fevereiro/recomendada-triagem-pre-natal-para-identificar-virus-que-pode-ser-transmitido-de-mae-para-filho-durante-a-amamentacao>

She listed some priorities: to continue offering training for health care professionals, to offer universal screening, to guarantee access to free infant formula, to expand and strengthen the multidisciplinary care of people living with HTLV (particularly pregnant women and exposed infants), to implement a notification system for HTLV surveillance. Increasing awareness among civil society is key to the inclusion of HTLV in the public health agenda. The recent participation of HTLVida, a civil society organization that represents people living with HTLV in Brazil, in the National Conference of Health was a successful example of the importance of engaging with civil society. At this opportunity the Ministry of Health and the Brazilian president collaborated to increase awareness about HTLV. The group has also engaged with politicians who are now willing to collaborate to advance the response to HTLV. Miranda finished her presentation affirming Brazil's willingness to include HTLV in its certification program for the elimination of mother-to-child transmission of HIV, syphilis, hepatitis, and Chagas disease.

Miranda was asked about the inclusion of HTLV in the recently launched interministerial committee for the elimination of tuberculosis and other socially determined diseases and the role of scientific and civil society to help to achieve this goal. She affirmed that the Ministry of Health is working towards this goal, with good expectations, particularly regarding prevention of mother-to-child transmission. Civil and scientific societies should continue the collaboration with the Ministry of Health and keep demanding progress in the response to HTLV to maintain HTLV in the agenda.

SAINT LUCIA: HTLV-1 SCREENING IN THE ANTENATAL CARE AND LEVERAGING THE EMTCT PLUS INITIATIVE

Dr. Gail Gajadhar, (Saint Lucia Ministry of Health, Wellness and Elderly Affairs), opened her talk with an overview of Saint Lucia, a Caribbean country with an estimated population of 178 692 individuals, 48 716 of whom are women of childbearing age. The country has around 2000 live births per year, and the number of pregnant women with HTLV varies annually (1-14 cases). Saint Lucia has implemented HTLV testing for blood donations, pregnant women (during the first test for pregnancy), and patients with STIs. They offer enzyme-linked immunosorbent assays (ELISA) for screening, followed by confirmatory test. Tests are free via the public health sector, but they are also available in the private sector. In the private sector, the test is costly. Pregnant mothers living with HTLV are counselled about HTLV and transmission routes, and they are advised not to breastfeed and to offer replacement (formula) feeding. Assistance is available if replacement feeding is unaffordable for those living with HTLV, similar to what is offered for mothers living with HIV. Saint Lucias prevention strategy relies on avoidance of breastfeeding, and data on HTLV-1/2 testing in pregnant women is collected along with HIV, syphilis, and Hepatitis B and C status.

The downside of Saint Lucia's response is the lack of follow-up for exposed infants and the lack of data collection for HTLV surveillance in blood donations and in the general population. In 2023, Saint Lucia launched universal health coverage. The first phase focused on maternal and child health services. Patients may access free wellness center visits and free blood tests for STIs (including HTLV). Phlebotomy is performed in wellness centers to improve access to blood tests. During its launch, awareness campaigns informed women of childbearing age about the available tests. The aim is to reduce the number of pregnant women who attend for delivery without a blood test. This would also contribute to achieve the targets proposed in the EMTCT Plus initiative.

During the discussion, Dr. Gajadhar affirmed Saint Lucia’s willingness to share its expertise and experience with other Countries to support a more effective response to HTLV in the Region. She affirmed that patients’ willingness to accept intervention to prevent HTLV transmission is high, similar to what is seen for HIV, which has resulted in the successful elimination of HIV mother-to-child transmission in the country since 2011. She also pointed out that the challenge of treating children and adolescents should be taken into account as an advantage of implementing strategies to prevent mother-to-child transmissions.

COLOMBIA: HTLV-1 DIAGNOSIS IN PEDIATRIC PATIENTS AND FOLLOW-UP OF EXPOSED INFANTS

After a general introduction on HTLV-1 and its associated diseases, Dr. Juan Rojas, of Universidad Libre Seccional Cali, Colombia, presented data on HTLV prevalence in Colombia. Most studies evaluated blood donors, and prevalence varied 0.03–0.18%. Higher prevalence was observed in studies of general population and indigenous communities. Dr. Rojas listed the possible clinical manifestations of HTLV-1 infection in pediatric patients (Table 1).

Table 1. Clinical manifestation of HTLV-1 infection in pediatric patients

	Symptoms:
Dermatological	Crusted scabies Infective dermatitis
Psychiatric	Depression
Nutritional	Severe malnourishment Impaired growth
Autoimmune	Autoimmune uveitis Rheumatoid arthritis Thyroiditis Polymyositis
Co-infections (opportunistic)	Tuberculosis Recurrent respiratory infections secondary to atelectasis Aspergillosis Recurrent strongyloidiasis <i>Mycobacterium leprae</i> HIV

In Colombia, confirmation of HTLV infection is usually done by WB as proviral load quantification is not widely available. Rojas highlighted the importance of international collaboration and technology transfer to improve Colombia’s diagnosis of HTLV. He shared his experience and a case series of pediatric patients with diverse clinical manifestation (uveitis, co-infection with Aspergillosis, tuberculosis). One patient presented with multiple co-infections. All pediatric patients diagnosed with HTLV-1 infection in his cohort were severely malnourished.

Regarding the laboratorial follow-up of exposed infants, Dr. Rojas proposed two algorithms, according to the feeding strategy. In babies who are exclusively formula-fed, he suggested testing infants at 18 months by PCR. If the test is negative, the medical team will decide if further testing is needed. If the test is positive, the medical team performs a second test (PCR or LIA). If the second test is positive, infection is confirmed. If not, the team assesses the need

for additional test(s). For babies who are breastfed, he suggested testing infants by PCR at 3, 6, 12, and 18 months of age. If negative at all time-points, the health care team will deliberate on the need for further tests. If positive, an additional PCR should be done within two to three months. If an infant has two positive PCRs, they should be considered infected by HTLV. If a second PCR is negative, the team should consult a specialist for advice to decide on the need for further testing.

There is no curative treatment for HTLV-1 infection, but Rojas called attention to the need for adequate nutritional monitoring for all infants living with HTLV and multidisciplinary follow-up according to the clinical manifestation. He also stressed the importance of considering the adoption of vaccination schemes for clinically vulnerable children of those living with HTLV-1. Clinical conditions should be observed before administering vaccines using live attenuated viruses. He suggested monitoring antibody response and considering the need for additional boost doses.

During the question and answer session, Rojas and the audience discussed the importance of diagnosing pediatric patients. While antenatal screening is important to provide counselling and care for pregnant women and prevent vertical transmission, some still question the importance of diagnosing pediatric patients. Rojas indicated the need to perform detailed clinical evaluations, including assessment of immune and nutritional impairment and of early signs of neurological diseases, as well as lifetime follow-up with hematologists and special vaccination programs. Pediatric diagnoses may also support mothers anxious to know if their infants were infected and to counsel these families about the virus and strategies to prevent transmission. From a programmatic perspective, pediatric diagnosis is important for the evaluation of a program focused on prevention of mother-to-child transmission.

ARGENTINA: IMPROVING HTLV-1 DIAGNOSTICS THROUGH INTERNATIONAL COLLABORATION

Why is HTLV a neglected infection? This question opened the presentation by Dr. Mirna Biglione (Consejo Nacional de Investigaciones Científicas y técnicas [CONICET]; Instituto de Investigaciones Biomédicas en Retrovirus y SIDA [INBIRS]; Universidad de Buenos Aires [UBA].) Comparing HTLV response to HIV response, Biglione observed the key difference: the role that civil society has played in advancing the response to HIV. The first step to improve diagnostics is to increase awareness about HTLV. HTLV prevalence and public health response is unequal globally. In many countries, epidemiological data are lacking or insufficient, and there are no central laboratories to offer confirmatory tests and HTLV-1/2 proviral load quantification. There are no protocols for molecular tests; no specialized care; no guidance for health care workers, vulnerable communities, or milk and gamete donors; and no guidance for public health response. Some countries are not testing blood donors for HTLV.

According to Biglione, knowledge transfer—accounting for national, regional, and linguistic differences and different degrees of complexities for different audiences—must improve. Strengthening the dialogue between countries—including academia, civil society, and people living with HTLV—is key to developing guidelines for diagnosis and treatment, to establishing networks to optimize laboratory protocols and quality control, to providing the foundation to develop a regional/international registration system, and to providing opportunities to share ideas and propose multicentric studies. The following offer examples of good practices: the Latin American group to study ATLL; Argentina’s publication of guidelines for diagnosis, notification and counselling of HTLV; the webpages <https://www.htlvaware.com> and <https://www.htlvconsciente.com> ; and the recently approved research project to strengthen the

articulation between countries. This project will offer online training on HTLV. The high number of registrations shows that the demand for knowledge is high.

When questioned about how PAHO and international agencies could support countries, Biglione pointed to the importance of producing simple international guidelines with experts from different countries. PAHO could facilitate international dialogue and engage local governments to encourage the inclusion of HTLV in their existing health programs, such as STI and maternal and child health programs.

CLOSING REMARKS

After acknowledging speakers and participants, Dr. Leandro Sereno from PAHO, recognized the importance of the discussions and affirmed that actions raised during the workshop align with PAHO's current work and perspectives. He agreed that increasing knowledge is key and reported that, in addition to the workshops, PAHO has been including HTLV in discussions with experts and with countries' representatives. There are still gaps in knowledge, but there is already enough evidence and tools to advance HTLV policies. Potential next steps include situational analysis of current practices in different countries, identifying and sharing good practices which are already implemented, and working towards the development of guidance to support countries strengthening their local response. PAHO is also working to identify opportunities for funds for HTLV research to help to close existing knowledge gaps.

CONCLUSION

There are sensitive and specific tests to diagnose HTLV infection, and countries are using local diagnostic algorithms. In some countries, algorithms are lacking. Coverage of HTLV screening is high among blood donors but still limited in antenatal care. International guidance on HTLV diagnosis, including on how to follow up exposed infants, would support local responses to HTLV and guide health care professionals. Low-cost point of care tests are in the pipeline and would facilitate the response to HTLV, particularly in the context of maternal and child health. There is a need to reduce the costs of testing and to improve access to testing, especially confirmatory tests. Saint Lucia has implemented policies to prevent HTLV mother-to-child transmission, and this response is integrated into the EMTCT Plus initiative. Chile, Brazil, and Colombia are progressing with their response to HTLV. The workshop provided opportunities to identify good practices and to delineate future directions, listed below.

Good practices:

- Saint Lucia's integration of HTLV into EMTCT Plus Initiative, with universal antenatal screening, intervention and surveillance;
- UK's simple guidance on HTLV diagnosis in pregnant women, including referral to specialized care and counselling;
- Chile's and Argentina's guidelines on HTLV care and mother-to-child transmission, to be launched soon;
- Brazil's patient engagement (HTLVida), contributing to increase awareness and the inclusion of HTLV in the political agenda;
- Chile's ongoing pilot study on antenatal screening and intervention to prevent mother-to-child transmission in high prevalence areas;

- Brazil's critical analysis of situational diagnosis of the response to HTLV and delineation of strategies to overcome barriers;
- Colombia's follow-up with pediatric patients living with HTLV, with the development of tentative diagnostic algorithm for exposed infants;
- Argentina's and Brazil's professional education about HTLV;
- Chile's strategy of offering antenatal screening tests regionally and confirmatory tests through a centralized laboratory.
- Chile's, Brazil's, and Saint Lucia's policy of complimentary infant formula for mothers living with HTLV;
- Brazil's and Chile's government financial support for research and Argentina's leverage of The Special Program for Research and Training in Tropical Diseases (TDR) and PAHO funds;
- Brazil's strong collaborative work done by different stakeholders;
- Saint Lucia's offering HTLV testing to people STIs;
- Regionally, high coverage of HTLV screening in blood donation in the Region.

Future directions::

- Include HTLV in the public health and political agenda by addressing HTLV in expert meetings with different groups and promoting discussion on topics related to this virus;
- Expand interest on HTLV, with advocacy at high levels in the ministries of health of Member States and international agencies;
- Increase awareness;
- Support and empower civil society so those living with the virus can actively contribute to strengthen, shape and advance policies to HTLV;
- Develop international guidance on HTLV diagnosis, including standardized operational protocol and quality assurance;
- Develop international guidance on preventing HTLV mother-to-child transmission, including counselling, prevention strategies and care, including targets and objectives;
- Improve training of health care professionals about HTLV diagnosis by providing courses and simple, clear local guidance on how to diagnose HTLV infection in pregnant women and exposed infants and to provide counselling and care;
- Establish and strengthen line of care for women living with HTLV and exposed infants;
- Support research on HTLV, especially on how to optimize diagnostic algorithm(s), to follow up on infection in infants, and to implement studies on strategies to improve coverage of HTLV screening and cost-effectiveness analyses;
- Facilitate safe and effective implementation of new technologies into clinical care;
- Encourage diagnostic companies currently offering platforms for large-scale testing for HIV viral load quantification to develop assays for HTLV proviral load detection and quantification;
- Strengthen collaboration between member states and facilitate technology transfer between and within countries;
- Work towards including HTLV into programs, such as EMTCT Plus, and the platform for the elimination of communicable diseases.

REFERENCES

1. Pan American Health Organization. The Response to HTLV in the framework of maternal and child health. Washington, DC: PAHO; 2022. Available from: <https://iris.paho.org/handle/10665.2/56888>.
2. Pan American Health Organization. International health policy forum for the elimination of HTLV. Washington, DC: PAHO;2021. Available from: <https://www.paho.org/en/international-health-policy-forum-elimination-htlv>
3. Rosadas C, Tosswill JH, Tedder R, Taylor GP. Pregnancy does not adversely impact diagnostic tests for HTLV-1/2 infection. *PLoS Negl Trop Dis*. 2019;13(9):e0007736. Available from: <https://doi.org/10.1371/journal.pntd.0007736>.
4. World Health Organization. Human T-lymphotropic virus type 1: technical report. Geneva: WHO;2021. Available from: <https://www.who.int/publications/i/item/9789240020221>.
5. Ministry of Health [Brazil]. Clinical management guide for HTLV infection [Guia de manejo clínico da infecção pelo HTLV]. Brasilia: Ministry of Health;2021. Available from: <http://www.aids.gov.br/pt-br/pub/2021/guia-de-manejo-clinico-da-infeccao-pelo-htlv>.
6. Ministry of Health [Chile]. Protocol for the treatment of patients with HTLV-1 [Protocolo de atención de pacientes con HTLV-i]. 2nd ed. Santiago: Ministry of Health;2018. Available from: <https://diprece.minsal.cl/wp-content/uploads/2019/10/PROTOCOLO-HTLV-definitiva-2da.-versión.pdf>.
7. Itabashi K, Miyazawa T, Sekizawa A, Tokita A, Saito S, Moriuchi H et al. A nationwide antenatal human T-cell leukemia virus type-1 antibody screening in Japan. *Front. Microbiol*. 2020;11: 595. Available from: <https://doi.org/10.3389/fmicb.2020.00595>.
8. Thorstensson R, Albert J, Andersson S. Strategies for diagnosis of HTLV-I and - II. *Transfusion*. 2002;42(6):780–91. Available from: <https://doi.org/10.1046/j.1537-2995.2002.00114.x>.
9. Herrera BB, Mayoral R, Brites C. Development and validation of a rapid screening test for HTLV-I IgG antibodies. *Viruses* 2022;15(1):129. Available from: <https://doi.org/10.3390/v15010129>.
10. Miranda AE, Rosadas C, Assone T, Pereira GFM, Vallinoto ACR, Ishak R. Strengths, weaknesses, opportunities and threats (SWOT) analysis of the implementation of public health policies on HTLV-1 in Brazil. *Front Med*. 2022;9. Available from: <https://doi.org/10.3389/fmed.2022.859115>.

ANNEX 1.

MEETING AGENDA

The diagnosis of human T-cell lymphotropic virus (HTLV) and strategies to expand HTLV screening in the context of Maternal and Child Health

Hour	Activity	
10 min	Welcome and opening remarks. - Dr Massimo Ghidinelli - Dr Carolina Rosadas - Mrs Angela Maria S Feitosa	Moderator: Leandro Sereno, PAHO PAHO HTLV Channel / Imperial College London Civil Society representative (Brazil)
15 min	HTLV diagnosis in pregnant women: State of the art and perspectives (current algorithms, performance of assays, cost, and challenges).	Prof. Graham Taylor Imperial College, United Kingdom
10 min	HTLV screening in blood banks (overview and strategies to improve service and surveillance in the Americas).	Mauricio Beltran Duran, PAHO
10 min	Discussion	
30 min	National experiences and perspectives: Chile: Current practices for blood donor screening and perspectives of antenatal screening. Brazil: Strategies to expand access to HTLV-1 diagnosis in Brazil. Saint Lucia: HTLV-1 screening in the antenatal care and leveraging on the EMTCT Plus Initiative.	Moderator: Carolina Rosadas, HTLV Channel/ Imperial College London Dr Jorge Valdebenito, Ministry of Health Chile Prof. Angelica Miranda, Ministry of Health, Brazil Dr. Gail Gajadhar, Ministry of Health, Sta Lucia
10 min	HTLV-1 diagnosis in pediatric patient and follow up of exposed infants.	Dr Juan Rojas, Universidad Libre Seccional Cali, Colombia
10 min	Improving HTLV-1 diagnostics through international collaboration.	Dr Mirna Biglione, CONICET, INBIRS, UBA, Argentina
10 min	Discussion	
	Final Comments and Closing	PAHO

In recent years, PAHO has been engaging with different stakeholders, including HTLV 1 specialists, health managers and people living with HTLV-1 to define priorities and to delineate effective strategies to tackle this neglected infection. One of the priorities identified by stakeholders is the prevention of HTLV-1 mother-to-child transmission. However, to be able to prevent vertical transmission, pregnant women living with HTLV-1 must be aware of their status. The coverage of HTLV-1 screening of blood donors is high in the Americas, but antenatal screening is still limited. Countries still face barriers to implement diagnostic tests for HTLV. There are no international guidelines for HTLV-1 diagnostics and national guidance may vary between countries. In this context, PAHO organized a workshop to discuss the diagnosis of HTLV-1 infection, particularly in the context of maternal and child health. Increased interest on HTLV-1 antenatal screening has been observed in the Americas and countries such as Chile, Brazil, St Lucia and Colombia shared their experience during the workshop. Good practices included the program to prevent HTLV-1 mother-to-child transmission, that is integrated with the EMTCT Plus initiative in St Lucia, strong collaboration between civil society, HTLV-1 experts and policymakers in Brazil, initiatives to increase awareness about HTLV-1 in the region and the construction of HTLV clinical guidelines by different countries in the region. Priorities identified include increasing awareness about HTLV, developing guidelines and support training of healthcare workers, strengthening the collaboration between countries and promoting the inclusion of HTLV into elimination programs.



Pan American Health Organization

525 Twenty-third Street, NW

Washington, D.C., 20037

United States of America

www.paho.org