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Prevalence of HTLV-1/2 infection in pregnant women in Central and South America and the Caribbean: a systematic review and meta-analysis

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ABSTRACT

Background: Human T-lymphotropic viruses (HTLV)-1 infection is endemic in many countries of Central and South America and Caribbean (CSA&C). Neither screening nor surveillance programs exist for HTLV-1/2 infection among pregnant women in this region. Neither in Western nations with large migrant flows from HTLV-1/2 endemic regions.

Methods: Systematic review and meta-analysis of the prevalence of HTLV-1/2 infection among CSA&C pregnant women. We included studies searching EMBASE, PubMed/MEDLINE, Scopus, and Web of Science from inception to February 15, 2023. This systematic review followed Preferred Reporting Items for Systematic Reviews and Meta-Analyses reporting guidelines.

Results: We identified a total of 620 studies. Only 41 were finally included in the meta-analysis. Most studies (61.0%) were from Brazil and Peru (14.6%). The total number of participants was 343,707. The pooled prevalence of HTLV-1/2 infection among CSA&C pregnant women was 1.30% (95% CI: 0.96-1.69) using anti-HTLV-1/2 antibody screening tests. There was a high heterogeneity ($I^2 = 98.6\%$). Confirmatory tests gave an HTLV-1 infection rate of 1.02% (95% CI: 0.75-1.33).

Conclusions: The prevalence of HTLV-1/2 infection among CSA&C pregnant women is 1.3%, most cases being HTLV-1. This rate is greater than for other microbial agents regularly checked as part of antenatal screening (such as HIV, hepatitis B, or syphilis). Thus, HTLV-1/2 antenatal testing should be mandatory among CSA&C pregnant women everywhere.

Introduction

Human T-lymphotropic viruses 1 (HTLV-1) and 2 (HTLV-2) were the first identified retroviruses in humans. Both were originally isolated from patients with T-cell leukemias or lymphomas in the early 1980s [1–3]. Soon thereafter, HTLV-1 was associated with the development of tropical spastic paraparesis in the Caribbean basin [4]. In contrast, HTLV-2 has only occasionally been linked to any disease since its first description [5].

Estimates for HTLV-1 are of at least 10 million people infected worldwide, with hotspots of endemicity recognized in Latin America [6], West and South Africa [7], Japan, Iran, Romania, and Australia [8]. In contrast, HTLV-2 is mostly recognized among injection drug users worldwide [9], some Amerindian tribes [10] and African pygmies [11]. A recent study reported the presence of HTLV-2 in 16

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indigenous people from the Brazilian Amazon region, highlighting the importance of breastfeeding and sexual transmissions [10].

The origin of HTLVs in South America shows at least two different branches with distinct entry timing. The major HTLV-1 entrance occurred through the east coast of Brazil at the beginning of the slave trade from the African continent, starting in the 16th century and lasting for more than 350 years. Previously, both HTLV-1 and HTLV-2 already had been introduced anciently, following human migrations from the Asian continent crossing the Behring Strait to the American continent and descending the Andes Mountains [12,13].

Both HTLV-1 and HTLV-2 are blood-borne transmitted viruses. However, because they are cell-associated, no transmissions occur following transfusion or exchange of plasma or plasma derivates, explaining why hemophiliacs or patients on hemodialysis are not infected. By far, sexual transmission is the most frequent way of HTLV-1 spreading globally [14,15]. HTLV-1 vertical transmission mostly occurs throughout breastfeeding and overall is recognized in up to 20-25% of newborns from infected mothers [16]. Children who are not breastfed beyond 3-6 months rarely become infected with HTLV-1 [17,18]. In spite of the efficacy of shortening or avoiding breastfeeding to stop HTLV-1 vertical transmission, antenatal screening is rarely performed in pregnant women in most HTLV-1 endemic countries.

Given that large migration flows from HTLV-1 endemic regions to Europe and North America have occurred during the last decades, reports of cases of HTLV-1-associated diseases are on the rise in Western countries. Furthermore, second waves of local transmission are also recognized among Western natives having sex partners from HTLV-endemic regions. For example, Spain has a 48 million population, Latin America being the largest migrant contributor with 2.7 million [19]. A total of 482 cases of HTLV-1 infection had been reported up to the end of 2023. Of note, 66% were Latin American, and mother-to-child transmission was recognized in at least 11% of cases [20]. In the United Kingdom, a recent survey estimated that 70 newborn infections because of HTLV-1 occur annually, most mothers being from the Caribbean basin [21]. The authors concluded that cost-effective analyses would support the efficacy of HTLV-1/2 antenatal testing, at least for pregnant women from endemic regions [22].

Herein, we perform a systematic review and meta-analysis of studies conducted so far on the rate of HTLV-1/2 infection in pregnant women of Central and South America and the Caribbean (CSA&C). This information should guide recommendations for HTLV-1/2 antenatal testing in endemic regions and in Western countries with significant migrant flows from such areas.

Methods

The systematic review was prepared following Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [23] (PRISMA checklist in supplementary material) and the protocol was registered at PROSPERO no. CRD42022315277 (https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022315277)

All publications recorded in international medical databases, including PubMed/Medline, EMBASE, SCOPUS, Web of Science, Scielo, and Cochrane, were checked until July 15, 2022. The search terms were chosen from the "Medical Subject Headings" (MeSH), using a combination of keywords. The first two authors examined independently each of the articles (Supplementary Table 1). Publications considered adequate were archived using the bibliographic 'Mendeley' platform (Elsevier). The search and selection step ended up on February 15, 2023.

Inclusion criteria for study selection were performed according to Population, Intervention, Comparison, Outcome (PICOS), as follows: i) Participants: pregnant women attended at antenatal sites in CSA&C; ii) Intervention: serological screening of HTLV-1/2 antibodies with subsequent confirmatory testing of initially reactive specimens; iii) Comparison: not needed; and iv) Results. Proportion of pregnant women infected with HTLV-1 or HTLV-2.

Further requirements in study design included being observational (cohorts or transversal) and specifying the number of persons included and tested. Articles had to be published in English, Portuguese, or Spanish.

Duplicated articles were identified and excluded, following the PRISMA procedure [23]. The full text of articles considered relevant was revised independently by two researchers before being considered adequate for further analyses. Differences in opinion were discussed and resolved by consensus with other investigators. All case series with less than five individuals were excluded from this analysis.

The first phase for the selection of articles to be examined was a reading of the title and abstracts. Two authors (JPS and ELG) independently reviewed their contents. Studies that did not reference HTLV, those reporting only clinical cases, those that did not include cohorts or cross-sectional studies, and those not conducted in CSA&C countries were excluded. In the second phase, all remaining articles were downloaded in full text, and a complete reading and examination were performed. We further excluded all studies that did not include confirmatory tests, were review articles, examined repeated patient populations, tested less than five patients, or did not specify how many patients included in the study tested positive for HTLV-1/2 (Figure 1). Disagreements during the first and second phases were resolved by consensus or researchers or by consulting an independent third party.

All relevant data from the articles chosen were recorded by two authors (JPS and ELG) using Excel. Another author (JMRR) checked the crude information. The following information was retrieved from the chosen articles: title, authors, publication year, study design, participants, age, ethnicity, country, education level, testing method, confirmatory assay, positive results, risk factors for transmission, HIV co-infection, and syphilis.

Two authors independently assessed the methodological quality of the studies included in the meta-analysis, using the 'Quality Assessment Tool for Case Series Studies' of the National Heart, Lung and Blood Institute (NHLBI) [24]. Disagreements were resolved by consensus or by asking an independent third party. The seven domains assessed were: bias because of confounding, bias in the selection of participants into the study, bias in the measurement of interventions, bias because of departures from intended interventions, bias because of missing data, bias in the measurement of outcomes, and bias in the selection of reported results.

Statistical analyses

All data were initially recorded in Excel (version Microsoft Office LTSC Standard 2021). All further analyses were performed using the Statsdirect software version 3.3.6 (StatsDirect Ltd Wirral, UK) (https://www.statsdirect.com).

A qualitative synthesis of all studies was initially performed. Then, a quantitative synthesis was then made using the Stuart-Ord method for proportion meta-analysis [25]. The estimates of HTLV-1/2 rates were graphically represented using forest plots, distinguishing HTLV-1/2 screening and confirmatory results. We used 95% CIs. The DerSimonian-Laird model was performed to assess the weight of distinct studies.

The heterogeneity between studies was assessed using the I2 index with 95% confidence intervals and the Cochran Q test. The I2 index ranges from 0 to 100%, considering *P*-values above 75% as too high. Publication bias was assessed using funnel plots, and

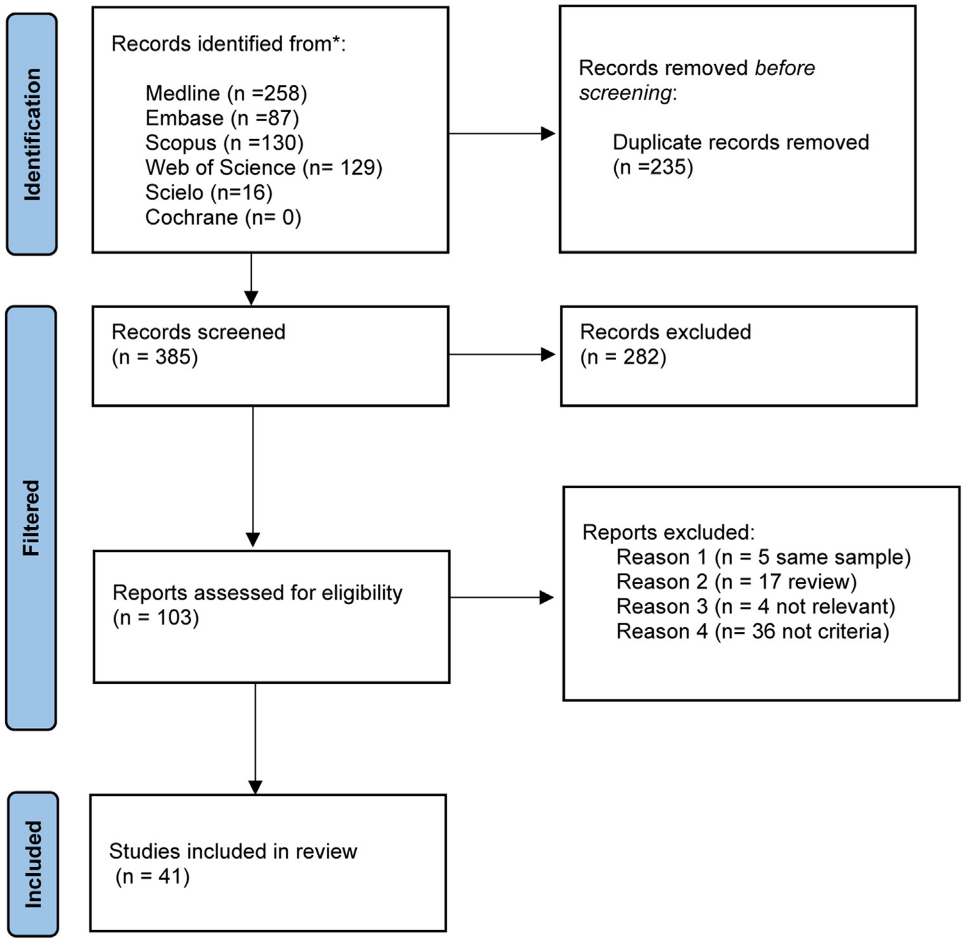

Figure 1. Flow diagram PRISMA 2020 for study selection.
[a]Consider, if feasible to do so, reporting the number of records identified from each database or register searched (rather than the total number across all databases/registers).
From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372: n71. http://dx.doi.org/10.1136/bmj. n71.
HTLV, Human T-lymphotropic viruses, PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

Egger and Harbord tests. Only *P*-values below 0.10 were considered adequate.

Results

A total of 620 articles were initially identified. After removing duplicates and small series, only 103 were selected. Full texts were retrieved, and further eligibility criteria were applied. Finally, 41 publications were chosen for the final meta-analysis (List of publications in Supplementary Table 2). The flow chart of the search is recorded in Figure 1.

All studies included in the meta-analysis had a transversal design and had been made in seven countries: 25 (61.0%) in Brazil, six (14.6%) in Peru, four (9.8%) in French Guiana, three (7.3%) in Argentina, two (4.9%) in Haiti, and one (2.4%) in Martinique. The main features of these studies are recorded in Table 1.

In the quality assessment, 36 studies were ranked as having good quality and five as fair quality (Supplementary Table 3).

The studies examined included a total of 343,707 pregnant women. Their mean age was 24.4 years, ranging from 12 to 50 years. The most frequent screening test for HTLV-1/2 antibodies were enzyme immunoassays (EIA) (n = 36; 87.8%), followed by chemiluminescence immunoassays (n = 4; 9.7%) and particle agglutination assay (n = 1; 2.4%). Besides the 1288 women who were confirmed as positive for HTLV-1, there were 189 additional women who were HTLV-1/2 seropositive but untypeable. Only 82 were confirmed as HTLV-2 positive.

Three studies did not report any positive cases of HTLV-1/2 screening and were excluded from the quantitative synthesis. In total, 38 studies were further analyzed. Overall, the rate of HTLV-1/2 positivity in the screening test was 1.30% (95% CI: 0.96-1.69) using a model of aleatory effects (Supplementary Figure 1). It presented high heterogenicity (I^2 = 98.6%; 95% CI = 98.5-98.7) and high asymmetry in the funnel plot (Figure 2), confirmed using the Egger's test ($p < 0.001$) (Supplementary Table 4).

HTLV-1/2 confirmatory tests were performed in 39 studies. The remaining two studies, both from Brazil, did not provide this information [56,64]. In 84.6% of the studies (34 of 39), a Western blot was used as confirmatory assay. polymerase chain reaction (PCR) was used in only three (7.7%) studies. In the rest, other tests were used, including Indirect Immunofluorescence (IFI) and Line Immuno Assay (Inno-LIA) HTLV I/II.

The rate of positive confirmatory results for HTLV-1 was 1.02% (95% CI: 0.75-1.33) using a model of aleatory effects (Figure 3). It depicted also a high heterogenicity (I^2 = 98.3%; 95% CI = 98.1-98.4) and high asymmetry in the funnel plot (Supplementary Figure 1), confirmed using the Egger's test ($p < 0.001$) (Supplementary Table 4).

Only 13 (32.5%) of studies (including 206,224 patients) reported cases of HTLV-2 infection (Table 1). These studies had been con-

Table 1
Main characteristics of studies included in the meta-analysis.

Author, year[a]	Country	Description of population	N	Median age (years)	Range (years)	Screening method	N (+)	Confirmation method	N (+)	N (+) HTLV-1	N (+) HTLV-2
Kline et al., 1991	Haiti	Women from Haiti as part of a perinatal study	1100	-	-	EIA	59	WB & RIPA	59	59	0
Wignall et al., 1992	Peru	Women attended in prenatal clinics in Lima (July 1987 to May 1988)	510	25.5	18-42	EIA	16	WB & RIPA	16	16	0
Allain et al., 1992	Haiti	Pregnant women who attended the hospital for prenatal care in three rural populations in northern Haiti (1988 and 1989)	500	25	15-49	EIA	11	WB & RIPA	11	11	0
Tuppin et al., 1995	French Guiana	Pregnant women belonging to different ethnic groups (July 1991 to June 1993)	1716	-	31-35	EIA	75	WB	68	68	0
Dos Santos et al., 1995	Brazil	Pregnant women referred to the public health laboratory of the state of Bahia for prenatal examination (November 1990 to June 1991)	1025	-	Categories (<21, 21-30 & >31)	EIA	15	WB	10	7	-
Lourerio et al., 1995	Brazil	Pregnant women	1000	-	14-40	EIA	16	WB	5	0	0
Broutet et al., 1996	Brazil	Six selected population groups, including pregnant women recruited from public health centers and hospitals (July 1993 to February 1994)	814	-	-	EIA	3	WB	2	1	1
Zurita et al., 1997	Peru	Pregnant women	211	-	15-49	EIA	5	WB	5	5	0
Mansuy et al., 1999	Martinique	Pregnant women receiving prenatal care at the Department of Maternity & Child Protection (August 1995 to January 1996)	467	26	15-49	EIA	9	WB	9	9	0
Tortevoye et al., 2000	French Guiana	Pregnant women from the regional public gynecology & obstetrics unit in Saint Laurent (July 1991 to June 1997)	3834	–		EIA	144	WB	144	144	0
Bittencourt et al., 2001	Brazil	Pregnant women who attended the prenatal care unit of a state maternity hospital in the city of Salvador (January 1996 to September 1998)	6754	26	Categories (14-20, 21-30 & 31-42)	EIA	61	WB & PCR	59	57	2
Carles et al., 2004	French Guiana	Pregnant women who gave birth in St. Laurent (July 1991 to June 1993)	1727	–	Categories (<21,21-25, 26-30, 31-35 & >36)	EIA	75	WB	75	75	0
Juscamaita et al., 2004	Peru	Pregnant women attending prenatal care and women at risk of sexually transmitted infections at the Regional Hospital of Ayacucho (November 2002 to February 2003)	602	-	Categories (<20,20-29, 30-39 & >40)	EIA	6	WB	3	3	0
Olbrich-Neto & Meira, 2004	Brazil	Embarazadas atendidas en Unidades Básicas de Salud del municipio de Botucatu.	913	-	–	EIA	2	WB	2	1	1
Figueiró-Filho et al., 2005	Brazil	Pregnant women attended Basic Health Units in the municipality of Botucatu	32512	-	Categories (15-19,20-29, 30-39 & 40-49)	EIA	37	WB & PCR	29	0	0
Tortevoye et al., 2005	French Guiana	Pregnant women who attended the sole regional public gynecology and obstetrics unit at the Saint Laurent du Maroni hospital (July 1991 to June 2001)	6331	27	Categories (<21, 21-25, 26-30, 31-35 & >36)	EIA	218	WB	218	218	0
Alarcon et al., 2006	Peru	Women who sought care at the Maternal Perinatal Specialized Institute (IMP) (August 1996 and April 1997)	2492	25.5	Categories (<20, 20-30 & >30)	EIA	42	WB	32	32	0

(*continued on next page*)

Table 1 (*continued*)

Author, year[a]	Country	Description of population	N	Median age (years)	Range (years)	Screening method	N (+)	Confirmation method	N (+)	N (+) HTLV-1	N (+) HTLV-2
Oliveira & Avelino, 2006	Brazil	All pregnant women attended all prenatal care units of the Municipal Health Department of Goiânia (September 2003 to December 2004)	15485	-	Categories (<30,& ≥30)	EIA	19	PCR	16	16	0
Eirin et al., 2007	Argentina	Pregnant women who attended two public hospitals in Buenos Aires and Neuquén	1867	-		EIA	3	WB	3	1	2
Trenchi et al., 2007	Argentina	Pregnant women registered in the public health service of the province of Córdoba (year 2000)	3143	-	–	PAA & IFA	171	WB	6	3	0
Fabbro et al., 2008	Brazil	Women seeking prenatal care in the Program for the Protection of Pregnant Women in the State of Mato Grosso do Su	116689	27	14-44	EIA	153	WB & PCR	150	133	17
Magalhães et al., 2008	Brazil	Pregnant women beyond 10 weeks of gestation in Cruz das Almas were randomly selected (June to October 2005).	408	-	14-32	EIA	4	WB	4	4	0
Ydy et al., 2009	Brazil	Puerperal women admitted at three public maternity hospitals affiliated with the Unified Health System in Cuiabá (April to September 2006)	2965	23.9	13-44	EIA	9	WB	7	6	1
Mello et al., 2009	Brazil	Pregnant women from the maternity ward of Vitória Mercy Hospital and the External Patient Referral Unit of the Municipality of Serra	447	24.8	12-44	EIA	6	IFA & MEIA	1	0	0
Souza et al., 2009	Brazil	Pregnant women were assisted during prenatal care in three public services in São Luis (February to December 2008).	2044	-	18-45	EIA	7	WB & PCR	7	4	3
Ribeiro et al., 2010	Brazil	Mothers and newborns. Samples collected on filter papers (September to November 2007)	55293	-	-	EIA	53	WB	42	40	2
Filho et al., 2010	Brazil	Consecutively attended pregnant women from the spontaneous demand of Faculdade de Medicina do Triângulo Mineiro (March to September 2008)	618	23.9	13-43	EIA	0	PCR	0	0	0
Sequeira et al., 2012	Brazil	Pregnant women interviewed during prenatal consultations at health units in 19 municipalities that entered the Maternal and Child Health program (February to November 2008)	13382	-	Categories (15-19, 20-39, & 40-49)	EIA	43	WB	41	39	1
Blas et al., 2013	Peru	Women from the Shipibo-Konibo ethnic group (July to December 2010)	1253	–	15-39	EIA	121	WB	121	74	47
Berini et al., 2013	Argentina	Pregnant women over 18 years old who attended prenatal consultations consecutively in five public hospitals	2403		>18	EIA	6	WB & PCR	6	3	3
Mello et al., 2014	Brazil	Women attended the prenatal units of the two regional hospitals (Ilheus and Itabuna) (November 2008 to May 2010)	2766	-	Categories (9-19, 20-29 & >30)	EIA	34	WB	29	29	0
Monteiro et al., 2014	Brazil	Pregnant women admitted for delivery at two public hospitals in the metropolitan area of Rio de Janeiro (November 2012 to April 2013)	1204	-	Categories (<24 & ≥ 25)	CMIA.	10	WB	8	7	1
Moura et al., 2015	Brazil	Pregnant women seeking care in the Universal Health System of Maceió during their first prenatal check-up (June 2007 to May 2012)	54798	23.3	15-35	EIA	129	WB	118	0	0

(*continued on next page*)

Table 1 (*continued*)

Author, year[a]	Country	Description of population	N	Median age (years)	Range (years)	Screening method	N (+)	Confirmation method	N (+)	N (+) HTLV-1	N (+) HTLV-2
Guerra et al., 2018	Brazil	Adolescent pregnant girls who attended prenatal care at the Specialized Unit for Maternal-Child and Adolescent Care (November 2009 to February 2010)	324	15.8	12-18	EIA	0	PCR	2	0	0
Mata et al., 2018	Brazil	Women of reproductive age in the urban area of Oiapoque	216	-	Categories (0-15, 16-20, 21-30, 31-40, 41-50)	EIA	0	WB	0	0	0
Costa et al., 2018	Brazil	Pregnant mothers who attended the Women's Reference Care Center (Maternidade Santa Helena) in the city of Ilhéus (July 2009 to July 2010).	511	–	13-44	EIA	6	WB & PCR	6	0	0
Medeiros et al., 2018	Brazil	Pregnant women attending a high-risk prenatal care unit at Clinical Hospital/Federal University of Paraná (August 2015 to August 2016)	643		18-47	CMIA	4	PCR	2	1	1
Barmpas et al., 2019	Brazil	Pregnant women attending a high-risk prenatal care unit at Clinical Hospital/Federal University of Paraná (August 2015 to August 2016)	1628	-	Categories (≤24 & >24)	CMIA	14	WB	12	0	0
Mendes et al., 2020	Brazil	Pregnant volunteers who were selected by free choice during the prenatal period at LACEN-MA (February 2015 to May 2017)	713	24.3	15-43	CMIA	5	WB & PCR	5	5	0
Vargas et al., 2020	Brazil	Parturient attended at two public maternity hospitals in Salvador, Bahia (April 2016 to June 2017)	2099	27.3	14-46	EIA	10	WB & PCR	9	0	0
Ramos et al., 2021	Peru	Pregnant women attending health centers in the city of Iquitos (May and June 2019)	300	26	≥18	EIA	5	WB & PCR	5	5	0

[a] List of publications in Supplementary Table 2.N, number; EIA, enzyme immunoassay; CMIA, chemiluminescence immunoassay; PAA, particle agglutination assay; IFA, indirect immunofluorescence assay; MEIA, microparticle enzyme immunoassay; WB, western blot; RIPA, radioimmunoprecipitation assay; PCR, polymerase chain reaction.

ducted in Brazil, Argentina, and Peru. None in the Caribbean or Central America. The rate of positive confirmatory results for HTLV-2 was 0.14% (95% CI: 0.06-0.25) using a model of aleatory effects (Figure 4). It had a high heterogenicity (I^2 = 94.2%; 95% CI = 92.2-95.4) and high asymmetry in the funnel plot (Supplementary Figure 1), confirmed using the Egger's test (p = 0.02) (Supplementary Table 4).

Discussion

In this systematic review and meta-analysis of HTLV-1/2 infection among pregnant women in CSA&C, we reported an overall prevalence rate of 1.02% (95% CI: 0.75-1.33) for HTLV-1 and of 0.14% (95% CI: 0.06-0.25) for HTLV-2. These rates significantly differ from those reported in a recent systematic review conducted on pregnant women in Brazil on studies published until mid-2020 [26], which found prevalence rates of 0.32% for HTLV-1 and 0.4% for HTLV-2 were found. The authors acknowledged a geographical split of HTLV-1 predominating in the north whereas HTLV-2 predominated in the southern regions.

In a study conducted in the late 90s among ethnic minorities living in South America [25], high rates of HTLV-1 were seen among the Peruvian Aymara (1.6%), the Bolivian Aymara (5.3%) and Quechua (4.5%), the Argentine Puna (2.3%), and the Chilean Atacama (4.1%). In contrast, HTLV-2 was highly prevalent among the Brazilian Kayapo (57.9%), the Paraguayan Chaco (16.4%), the Chilean Alacalf (34.8%), and Yahgan (9.1%). Accordingly, the authors concluded that there was a geographic clustering of HTLV-1 foci in the Andes highlands and of HTLV-2 foci in the lowlands of South America.

In our study, high rates of HTLV-1 (1%) were uniformly noticed in all studies conducted on pregnant women in Caribbean countries, such as Haiti, Martinique, and French Guiana. Interestingly, none reported a single case of HTLV-2 infection. In contrast, we recorded pregnant women with HTLV-2 infection in Brazil and Argentina, generally with low rates and nearly always below those seen for HTLV-1 in these countries. Intriguingly, one exception was one study conducted on pregnant women from the Shipibo-Konibo ethnic minority living in the Peruvian Andes, which reported a 4% rate of HTLV-2 along with a 7% of HTLV-1 infection (Blas et al., 2013 in Table 1)

There was a high heterogeneity between studies included in our meta-analysis. Accordingly, HTLV-1/2 rates differed substantially. A large proportion of women examined belonged to special populations, including ethnic minorities, rural areas, and well-known highly HTLV-1/2 prevalent regions. In contrast, a few studies included women from urban areas with null or low Amerindian ancestry. As expected, in the latter studies HTLV-1/2 prevalence rates

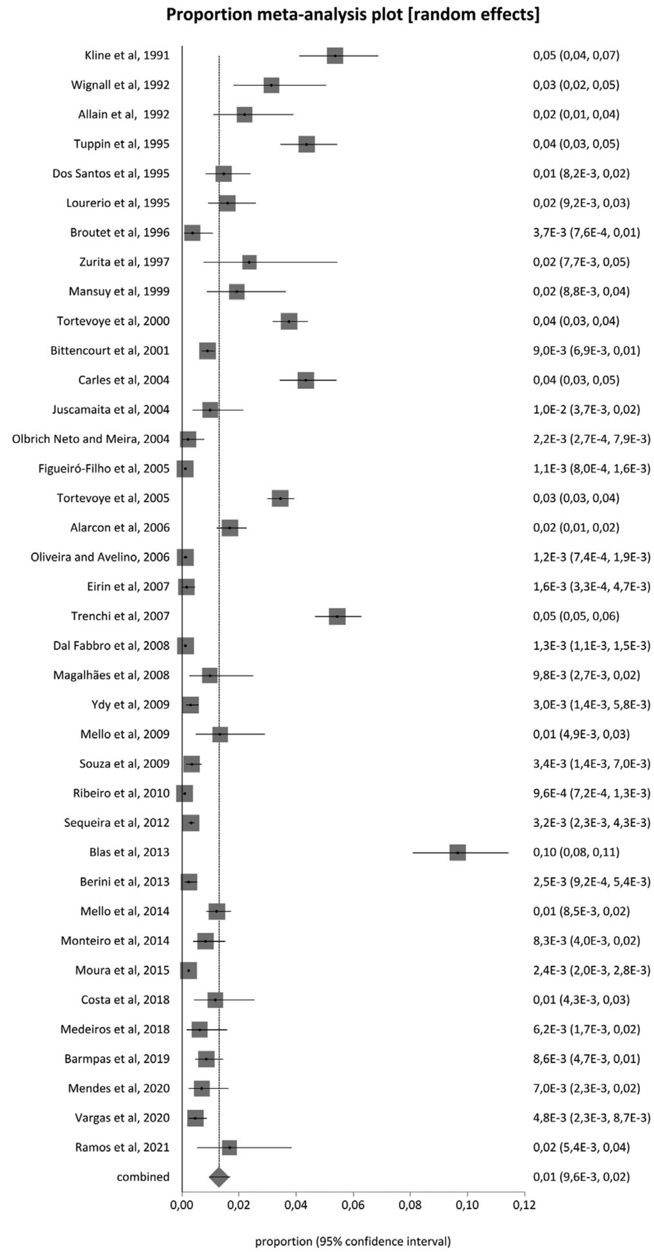

Figure 2. Pooled prevalence of HTLV-1/2 positivity in the screening test.
HTLV, Human T-lymphotropic viruses.

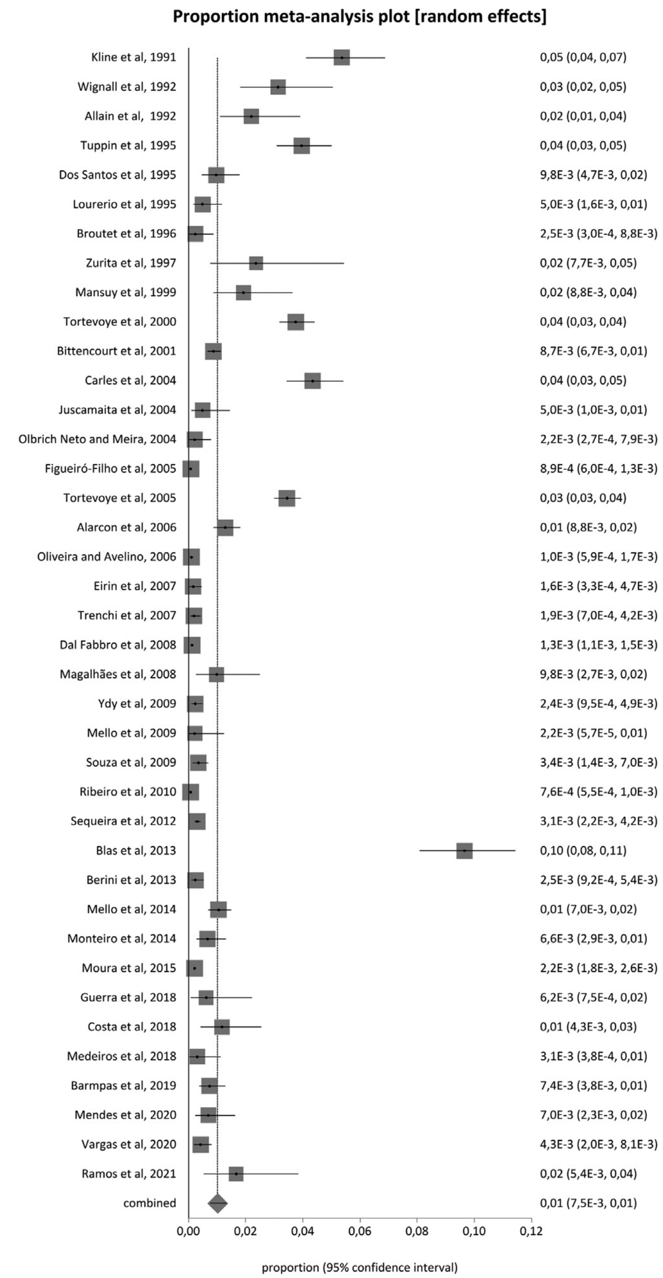

Figure 3. Pooled prevalence of positive confirmatory results for HTLV-1.
HTLV, Human T-lymphotropic viruses.

were significantly lower. In some studies, from Brazil (Table 1: Filho et al., 2010, Guerra et al., 2018 and Mata et al., 2018), no pregnant women with HTLV-1/2 infection were found.

An interesting finding in our study refers to the relatively good performance of HTLV-1/2 screening assays, with an average 90% confirmation of initially seroreactive samples. The fact that the study population was expected to depict moderate to high rates of HTLV infection could explain this finding. Most concerns about false positive rates came from studies performed in low-risk populations in non-endemic regions, such as blood donors in Europe or North America [27].

Limitations

We should acknowledge several caveats in our meta-analysis. Firstly, we could not find any study from continental Central America that fitted the inclusion criteria, so such a region was not represented in this systematic review. Of note, only studies from four countries in South America and another four in the Caribbean basin were examined. Again, misrepresentations of other countries could influence our results. Secondly, the reliability of HTLV-1/2 assays was quite variable comparing distinct tests and periods, as previously highlighted by others [28]. Although we considered both screening results along with confirmatory results, a substantial proportion of women gave HTLV-1/2 positive results on immunoblot that were untypable. Because PCR was not performed, these serological results should be interpreted cautiously. In this regard, misdiagnosis of HTLV-1 and in less extent of HTLV-2 might have occurred to some extent. Both in the pooled analysis of the screening and confirmatory results, asymmetrical funnel plots can be observed (Supplementary Figs 1-C). This is explained by the fact that prevalence results below 0 are not possible. Therefore, neither the plots nor the results of the bias tests necessarily indicate pub-

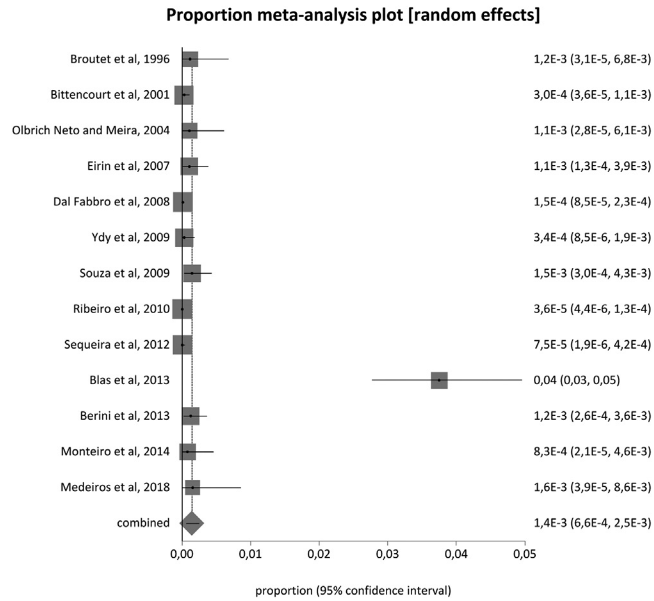

Figure 4. Pooled prevalence of positive confirmatory results for HTLV-2. HTLV, Human T-lymphotropic viruses.

lication bias [29]. In contrast, we attribute the high heterogeneity found not only to the intrinsic differences between the studies but also to the fact of counting and pooled estimates <10% and a high number of studies. The last observation is that the prevalence of newborns testing positive for HTLV-1/2 was not evaluated, even though the original study design was intended to investigate these results. Conducting studies such as the present systematic review and meta-analysis is important for evaluating the prevalence of vertical HTLV transmission.

Conclusions

This meta-analysis and systematic review show a 1.3% rate of HTLV-1/2 infection among pregnant women in SCA&C. This figure is greater than rates for HIV, syphilis, or hepatitis B, for all of which there is a clear recommendation for antenatal testing. Thus, our results support the introduction of HTLV-1/2 screening of pregnant women from CSA&C everywhere. This recommendation is particularly relevant for endemic regions but also extends to Western countries with a significant CSA&C migrant population.

Declarations of competing interest

The authors have no competing interest to declare.

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Ethical approval

The meta-analysis study is exempt from ethics approval, as the study authors collected and synthesized data from previously published studies.

Authors contributions

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Availability of data and materials

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijid.2024.107018.

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