Original Article

PD-L1 expression in non-small cell lung carcinoma in Latin America: a systematic review and meta-analysis

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Background: Programmed cell death ligand 1 (PD-L1) expression in non-small cell lung carcinoma (NSCLC) is a crucial factor in predicting responses to immunotherapy. This systematic review and meta-analysis focuses on the prevalence of PD-L1 expression and clinicopathological features among Hispanic/Latino (H/L) populations.

Methods: Embase, LILACS, Medline, and Virtual Health Library were searched for studies that evaluated the prevalence of PD-L1 in H/L patients. The protocol was submitted to PROSPERO with ID CRD42023488547. We employed the Joanna Briggs Institute Checklist for Systematic Reviews and Research Syntheses to assess the methodological quality and applicability of the included studies. Meta-analyses were done to determine the prevalence using a random effects model.

Results: The meta-analysis, encompassing 21 articles with 16,486, revealed that 80.2% of patients had PD-L1 expression data available (n=13,222). The prevalence calculated of PD-L1 expression in Latino NSCLC patients was 55% [95% confidence interval (CI): 0.54–0.55], with 31% (95% CI: 0.27–0.36) showing a tumoral proportion score (TPS) of 1–49%, and 23% (95% CI: 0.16–0.30) registering a TPS ≥50%. Higher expression was observed in male gender, smoking, adenocarcinoma subtypes, poor tumor differentiation, and advanced stages. PD-L1 expression was most frequent in *EGFR* wild-type status (82.5%) with a odds ratio (OR) 1.54 (95% CI: 1.24–1.92) and PD-L1 expression was associated with *ALK* positive (OR =1.54; 95% CI: 1.24–1.92).

Conclusions: This meta-analysis provides a comprehensive overview of PD-L1 expression in NSCLC in the H/L population. The findings underscore the significant prevalence of PD-L1 expression and emphasize the relevance of immunotherapy in this population. Understanding the clinicopathological features associated with PD-L1 expression can contribute to tailored treatment strategies for NSCLC in Latin America.

Keywords: Lung; cancer; programmed cell death ligand 1 (PD-L1); Latin America; prevalence

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Introduction

Lung cancer is the second most diagnosed neoplasm globally and the leading cause of cancer-related deaths. In Latin America and the Caribbean, it ranks as the third most common cancer after prostate and breast cancer, with 97,601 new cases annually, and remains the leading cause of cancer deaths, claiming 86,627 lives each year (1). Recent years have seen significant advancements in clinical outcomes due to the identification of oncogenic driver mutations and the expression of programmed cell death ligand 1 (PD-L1), which have become standard-of-care due to improved clinical outcomes (2,3).

Programmed cell death 1 receptor (PD-1) and its ligand PD-L1 play an important role in physiological immune homeostasis and are involved in the pathway through which cancer cells evade the immune system (4). PD-1 is expressed on the cell surface of T and B cells, natural killer cells, macrophages, dendritic cells, and monocytes. PD-L1 is commonly expressed by macrophages, certain activated T cells, B cells, dendritic cells, and some epithelial cells, especially under inflammatory conditions and in malignant cells. The binding interaction between PD-1 and PD-L1 results in the inhibition of T cell activation, migration, proliferation, survival, and cytotoxic secretion within cancer cells (4,5). The humanized antibody blockade of PD-1/PD-L1 reverses the binding of this process and enhances antitumor immune activity. These immune checkpoint inhibitors (ICIs) have changed the treatment for many tumors with different clinical indications (6).

Currently the expression of PD-L1 is tested by immunohistochemistry (IHC) mainly on formalin-fixed paraffin-embedded (FFPE) histological specimens. Three scores are used by the pathologists depending on the malignant tumor, antibodies (28-8, 22C3, SP142, SP263), and clinical treatment. These scores are tumoral proportion score (TPS), combined positive score (CPS), and immune cell score (IC). Some tumors are positive with scores of ≥1 and others with scores of ≥10. In non-small cell lung carcinoma (NSCLC) the expression of PD-L1 is divided into <1%, 1–49%, and ≥50% and the clones used in the clinical practice are 22C3 and SP263 (7).

Several challenges to the implementation of molecular testing and treatment for NSCLC have been seen in Latino patients (8,9). Currently, checkpoint inhibitors (PD-L1) and some targeted therapies (*EGFR*, *ALK*, *ROS1*, *KRAS*, *NTRK*) are approved for NSCLC in Latin America (9). Recently, in a systematic review we observed that the prevalence of actionable mutations in the Latino population was different than it is in the Caucasian and Asian populations (10). The goal of the present article is to determine the prevalence of PD-L1 expression and clinicopathological features in the Hispanic/Latino (H/L) population with NSCLC. We present this article in accordance with the PRISMA reporting checklist (11) (available at https://tlcr.amegroups.com/article/view/10.21037/tlcr-24-223/rc).

Highlight box

Key findings

- This meta-analysis examined 21 articles covering 16,486 Hispanic/Latino (H/L) patients with non-small cell lung carcinoma (NSCLC). It was found that 55% of these patients exhibited programmed cell death ligand 1 (PD-L1) expression, with 31% showing a tumoral proportion score (TPS) of 1–49% and 23% with a TPS of 50% or higher.

What is known and what is new?

- Higher levels of PD-L1 were associated with male patients, smokers, adenocarcinoma subtypes, poor tumor differentiation, and advanced disease stages. The expression was most prevalent in patients with EGFR wild-type status and also significantly associated with ALK positivity.
- This study provides new data on the prevalence and implications of PD-L1 in H/L populations, a group often underrepresented in medical research, highlighting specific patterns of expression linked to various clinicopathological features.

What is the implication, and what should change now?

- The significant prevalence of PD-L1 expression indicates that a considerable portion of the H/L NSCLC population could benefit from targeted immunotherapies. The findings advocate for the routine implementation of PD-L1 testing in the diagnostic and therapeutic strategies for these patients to enhance personalized treatment approaches. Policies should also be adapted to ensure access to such diagnostics and treatments, promoting better health outcomes in this population.

Methods

The protocol was submitted to PROSPERO, the International Prospective Register of Systematic Reviews, under the number CRD42023488547.

Inclusion criteria

The inclusion criteria for the systematic review encompassed descriptive studies, cohorts, and clinical trials assessing the

frequency of PD-L1 expression using antibodies 22C3 or SP263 in H/L patients. Articles published up to April 2024 were considered, regardless of language. When the same population was reported in multiple articles, those with the highest number of cases were selected.

Exclusion criteria

The following exclusion criteria were applied: (I) studies with inconsistencies between the text and table results; (II) studies that included patients with a specific driver mutation.

Information sources and search strategy

Detailed, tailored search strategies were employed for each of the following electronic databases: Embase, LILACS, Medline, and the Virtual Health Library. Grey literature was also retrieved using Google Scholar. All searches were conducted in April 2024. Additionally, a hand search, expert consultations, and a review of reference lists from selected articles were performed. Appropriate truncations and word combinations were applied and adjusted for each database (Table S1). Terms considered included: cancer, neoplasms, Hispanic or Latino, Spanish Origin, Latin America and anti-PD-L1. The term "Hispanic or Latino" is currently defined as a person of Cuban, Mexican, Puerto Rican, South or Central American, or other Spanish culture or origin, regardless of race. Latino patients do not necessarily come geographically from Latin America, and it is well known that in the Central and South American territory there is a significant racial and ethnic variety. Despite the above, in this review we will speak indistinctly of Hispanic or Latino referring to race based on the geographic origin of the patients.

Study selection

The eligibility of the selected articles was assessed in two phases. In phase 1, five authors (J.P.C.G., L.M., M.P.V., D.C.C., M.P.G.G.) independently screened the studies by title and abstract. In phase 2, the same authors reviewed the abstract and full text of all screened articles, excluding those that did not meet the inclusion criteria. Any disagreements were resolved by consulting another author (R.P.M.). References from relevant articles were manually searched. All included data were reviewed by the authors. The final selection was based on the full text of the publication or the abstract of the conference presentation.

Data collection process and data extraction

The following data were extracted from each article when available: author name, country of origin of the patients, year of publication, recruitment period, number of patients, PD-L1 expression categorized as <1%, 1–49%, and ≥50%, and clinical data including age, smoking status, sex, histological subtype, disease stage, metastasis, and Eastern Cooperative Oncology Group (ECOG) score. Additionally, associated mutations of *EGFR*, *ALK* and *KRAS* were recorded based on data availability. Disagreements were resolved by consensus. If the required data were incomplete, efforts were made to contact the authors for the missing information.

Risk of bias and applicability

To evaluate the methodological quality and applicability of the included studies, a checklist based on the Joanna Briggs Institute Critical Appraisal Checklist for Systematic Reviews and Research Syntheses (12) was utilized. Two reviewers (J.P.C.G., M.P.V.) independently assessed each study, answering eight questions for cross-sectional studies and 11 questions for cohort studies. Responses to each question were categorized as 'yes' (Y), 'no' (N), 'unclear' (U), or 'not applicable' (NA).

Summary measures

The primary outcome was the prevalence or incidence of PD-L1 expression. Prevalence was calculated as patients with mutations divided by <1%, 1–49%, and ≥50%.

Data synthesis and analysis

All quantitative analyses of the included studies were conducted in R using the metafor and meta packages. Meta-analyses were performed using a random effects model to determine the prevalence of PD-L1 expression. Heterogeneity was evaluated using the I^2 statistic, with values greater than 75% indicating high heterogeneity. The significance level was set at 5%. Heterogeneity was further

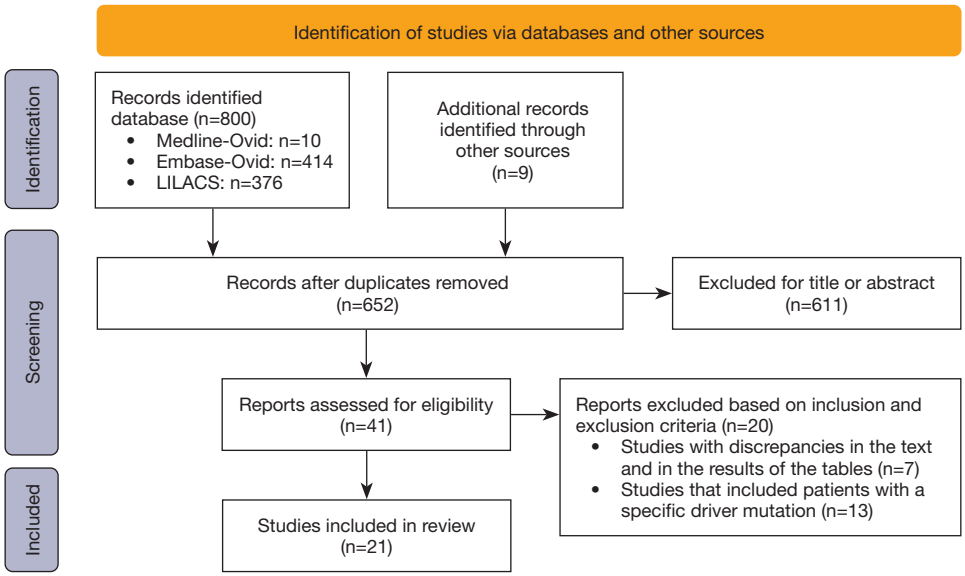

Figure 1 Flow chart in the systematic review.

assessed based on sample size, country, and study design.

Results

General search results

A total of 809 original articles were identified, with 157 being duplicates. After screening titles and abstracts, 611 articles were rejected. Ultimately, 21 articles met the inclusion and exclusion criteria and were included in the review (13-33) (*Figure 1*).

In the case of seven articles (13,15,18-21,24) data were extracted from the abstract. Three multicenter studies were found in different countries. Two of them were based on records from the Latin American Consortium for Lung Cancer Research (CLICaP) (22,23) and the remaining ones came from the Latin American Cooperative Oncology Group (LACOG) (24). The information was extracted by country. Among the single-center studies, six articles from Brazil (14,25,27-30), four from Colombia (15,31-33), two from Mexico (17,18), and Argentina (13,26) one each from Ecuador (16), and Peru (19) were found. Two articles included Latinos residing in the USA (20,21). All the studies were published between 2017 and 2022.

General clinical information

Clinical and sociodemographic data were extracted from 19 articles (n=14,244). Information on age was available in 15 of the articles (n=12,787) and information on sex could be extracted from 16 manuscripts (n=13,364) (*Table 1*). The median age reported was 65.5 years and 55.2% were male (n=7,373/13,364). Regarding smoking status, 73.8% (n=2,971/4,025) were found to be smokers. It was possible to report information on the histological subtype of NSCLC in 13,072 patients and lung adenocarcinoma (LUAD) was found to be the most frequent (71%, n=9,285) followed by lung squamous cell carcinoma (LUSC) (12%, n=1,573) and adenosquamous carcinoma (4.2%, n=550).

The clinical stage of NSCLC was reported in 1,443 patients and half of the cases were stage IV (46.5%, n=681). Stages IIIA (17.7%, n=259), IIIB (12.9%, n=189), IIB (7.65%, n=112), IB (6.63%, n=97), and IIA (5.46%, n=80) were reported in smaller proportions. The other stages presented a frequency of less than 5%. When the information related to the presence of metastases was evaluated, 583 patients presented metastatic primary NSCLC. The most frequently affected by metastases organs were the lungs (lung-to-lung metastases) (52.8%, n=308), followed by the brain (38.6%, n=225), bones (5%, n=29), and liver (3.3%, n=19). The site of metastasis was not clearly reported for two patients (0.3%). Most Latino patients with NSCLC were classified as ECOG 1 (63.9%, n=956/1,496), followed by ECOG 0 (18.9%, n=283/1,496), ECOG 2 (11.7%, n=175/1,496), ECOG 3 (5%, n=75/1,496), and ECOG 4 (0.5%, n=7/1,496). The type of treatment received was reported for 323 patients. Conventional chemotherapy

Table 1 Clinical characteristics of patients included with lung cancer by country

Clinical characteristics	Argentina	Brazil	Colombia	Ecuador	Mexico	Peru	H/L in US	Multicentric[†]	Total, n (%)
Number of patients evaluated PD-L1	9,016	2,622	556	79	747	82	131	1,011	14,244
Age (years)									
Median	65.5	66.5	66.4	–	–	65	–	64.4	65.5
Mean	–	–	66	58.8	64	–	–	64.8	63.4
Sex									
Female	3,801	1,262	219	52	409	32	73	143	5,991 (44.8)
Male	5,176	1,360	223	27	338	50	58	141	7,373 (55.2)
Smoking history									
Yes	1,334	292	250	13	219	31	93	739	2,971 (73.8)
No	325	101	168	57	265	51	38	49	1,054 (26.2)
Histology type									
Adenocarcinoma	6,427	1,273	385	56	712	69	106	257	9,285 (71.0)
Squamous cell carcinoma	1,173	255	123	4	–	–	–	18	1,573 (12.0)
Adenosquamous carcinoma	29	95	3	–	–	–	–	423	550 (4.2)
Poor differentiated carcinoma								4	4 (0.03)
Carcinoma NOS	1,287	287	11	–	–	–	–	1	299 (12.2)
Other histology	8	35	12	19	–	–	–		66 (0.6)
Disease stage									
IA	–	–	7	–	–	–	–	–	7 (0.47)
IB	–	92	5	–	–	–	–	–	97 (6.63)
IIA	–	73	7	–	–	–	–	–	80 (5.46)
IIB	–	103	9	–	–	–	–	–	112 (7.65)
IIIA	–	214	25	–	–	–	–	20	259 (17.7)
IIIB	–	121	24	–	–	–	–	44	189 (12.91)
IIIC	–	–	2	–	–	–	–	16	18 (1.23)
IV	–	176	426	79	–	–	–	–	681 (46.54)
Not known	–	–	20	–	–	–	–	–	20 (1.36)
Metastases									
NOS	–	–	2	–	–	–	–	–	2 (0.34)
Bone	–	14	3	12	–	–	–	–	29 (4.97)
Liver	–	2	3	14	–	–	–	–	19 (3.25)
Brain	–	4	2	14	–	–	–	205	225 (38.5)
Lung	–	270	17	21	–	–	–	–	308 (52.83)

Table 1 *(continued)*

Table 1 *(continued)*

Clinical characteristics	Argentina	Brazil	Colombia	Ecuador	Mexico	Peru	H/L in US	Multicentric[†]	Total, n (%)
Management									
TKI (1st gen)	–	–	–	–	–	–	–	80	80 (24.76)
TKI (2nd gen)	–	–	–	–	–	–	–	–	–
TKI (3rd gen)	–	–	–	–	–	–	–	–	–
Immunotherapy	–	–	–	–	–	56	–	–	56 (17.33)
Combination with chemotherapy	–	107	–	–	–	–	–	80	187 (57.89)
Functional patient status									
ECOG 0	–	107	55	7	–	63	–	51	283 (18.91)
ECOG 1	–	141	592		–	12	–	211	956 (63.9)
ECOG 2	–	16	92	67	–	–	–	–	175 (11.7)
ECOG 3	–	7	46	–	–	–	–	22	75 (5.0)
ECOG 4	–	–	7	–	–	–	–	–	7 (0.46)
Survival (months)									
Overall survival, median	–	–	23.3	–	–	–	–	26	24.6
Progression-free survival, median	–	–	–	–	–	–	–	19.4	19.4

[†], included patients from Mexico, Colombia, Costa Rica, Argentina, Chile, Peru, Brazil, H/L in US. H/L, Hispanic/Latino; PD-L1, programmed cell death ligand 1; NOS, not otherwise specified; TKI, tyrosine kinase receptor inhibitor; gen, generation; ECOG, Eastern Cooperative Oncology Group.

was given to 57.9% (n=187) of the patients and, of these, 80 patients received additional therapy with first-generation tyrosine kinase receptor inhibitors (TKIs). Of the total number of patients, 17.3% (n=56) received immunotherapy.

Clinical information on PD-L1-positive patients

Clinical and sociodemographic of patients with the PD-L1 expression evaluated were extracted from nine articles (n=11,526) (*Table 2*) (13,17,25-28,30-32). The mean age reported in this group was 65 years and 56.4% were male. Most patients were exposed to tobacco (73%).

The most frequent histological subtypes were adenocarcinoma, 68.4% (n=3,971/5,808) followed by squamous cell carcinoma, 15.4% (n=895/5,808). Among the adenocarcinomas, the predominant pattern in this subgroup of patients was reported in 187 cases. The most frequent pattern found was solid (66.8%, n=125/187), followed by the papillary (12.8%, n=24/187), acinar (8.6%, n=16/187), lepidic (8.6%, n=16/187), micropapillary (1.6%, n=3/187) and mucinous (1.6%, n=3/187) patterns. Regarding the oncological stage, 44.2% of the patients were stage IIIA (n=42/95) followed by 19% (n=18/95) stage IV, 17.9% (n=17/95) stage IIB, 10.5% (n=10/95) stage IB, 4.2% (n=4/95) stage IIA and 4.2% stage IIIB. One study evaluated expression in early stages (IB to IIIA-AJCC seventh edition) and found higher expression in stages IIB/IIIA (30). Forty-seven patients had metastases in the same lung, and 59.7% and 40.3% had an ECOG score of 1 and ECOG 0 respectively.

Frequency of PD-L1 expression in Latin American patients

Of the 21 articles included (n=16,486), 13,222 patients (80.2%) were evaluated for PD-L1 expression. The meta-analysis found a 55% [95% confidence interval (CI): 0.54–0.55] prevalence of PD-L1 in Latino patients with NSCLC. The prevalence was 31% (95% CI: 0.27–0.36) for subjects with TPS expression 1–49% and 23% (95% CI: 0.16–0.30) for TPS expression ≥50% (*Figure 2*).

A sensitivity analysis that excluded articles that evaluated PD-L1 expression in patients with squamous cell carcinoma of the lung [Cardona *et al.* (31) and Fernández-Trujillo *et al.* (32)] was done. No significant changes in prevalence were seen

Table 2 Clinical characteristics of patients included with lung cancer and PD-L1 evaluated

Clinical characteristics	PD-L1 (+), n [%]/n	PD-L1 (–), n [%]/n
Number of patients evaluated	6,098 [52.9]	5,428 [47.1]
Age (years), median	65	66
Sex	n=6,097	n=8,251
Female	2,658 [43.6]	2,372 [28.8]
Male	3,439 [56.4]	5,879 [71.2]
Smoking history	n=1,258	n=994
Yes	918 [73]	698 [70]
No	340 [27]	296 [30]
Histology type	n=5,808	n=5,026
Adenocarcinoma	3,971 [68.4]	3,800 [75.6]
Squamous cell carcinoma	895 [15.4]	565 [11.3]
Adenosquamous carcinoma	18 [0.3]	11 [0.2]
Poor differentiated carcinoma	–	–
Carcinoma NOS	924 [15.9]	650 [12.9]
Other histology	–	–
Histological subtype	n=187	n=351
Acinar	16 [8.6]	144 [41]
Lepidic	16 [8.6]	32 [9.1]
Micropapillary	3 [1.6]	1 [0.3]
Mucinous	3 [1.6]	10 [2.8]
Papillary	24 [12.8]	46 [13.1]
Solid	125 [66.8]	118 [33.6]
Disease stage	n=95	n=130
IA	–	–
IB	10 [10.5]	39 [30]
IIA	4 [4.2]	24 [18.5]
IIB	17 [17.9]	12 [9.2]
IIIA	42 [44.2]	49 [37.7]
IIIB	4 [4.2]	1 [0.8]
IIIC	–	–
IV	18 [19]	5 [3.8]
Not known	–	–
Metastases		
NOS	–	–
Bone	–	–
Liver	–	–
Lung	47	75
Functional patient status	n=57	n=104
ECOG 0	23 [40.3]	48 [46.1]
ECOG 1	34 [59.7]	56 [53.9]
ECOG 2	–	–
ECOG 3	–	–
ECOG 4	–	–
Overall survival (months), median	24.8	–

PD-L1, programmed cell death ligand 1; NOS, not otherwise specified; ECOG, Eastern Cooperative Oncology Group.

(51%, 95% CI: 0.42–0.59), nor were they seen in the patients with TPS 1–49% (31%, 95% CI: 0.26–0.36) and with ≥50% (22%, 95% CI: 0.15–0.30) (Figure S1).

Frequency of PD-L1 expression and presence of molecular alterations

Seven articles were found that evaluated both the PD-L1 expression and the presence of mutation in the *EGFR* gene together (13,15,17,19,26,28,30). Within those reporting PD-L1-positive TPS (n=4,500), there were 787 *EGFR*-positive patients (17.5%) and 3,713 *EGFR*-negative patients (82.5%). In contrast, there were 3,484 patients that did not have PD-L1 expression, and of these, 22.8% were *EGFR* positive (n=794) and 77.2% were *EGFR* negative (n=2,690). The analysis found an association between the PD-L1 expression and *EGFR* negative [odds ratio (OR) =1.54; 95% CI: 1.24–1.92].

The expression of PD-L1 with the presence of molecular alterations of the *ALK* gene was described in five articles (15,17,25,26,28). Of these patients, 4,324 were found to have positive PD-L1 expression and 3,610 were found to have no PD-L1 expression. The proportion of ALK

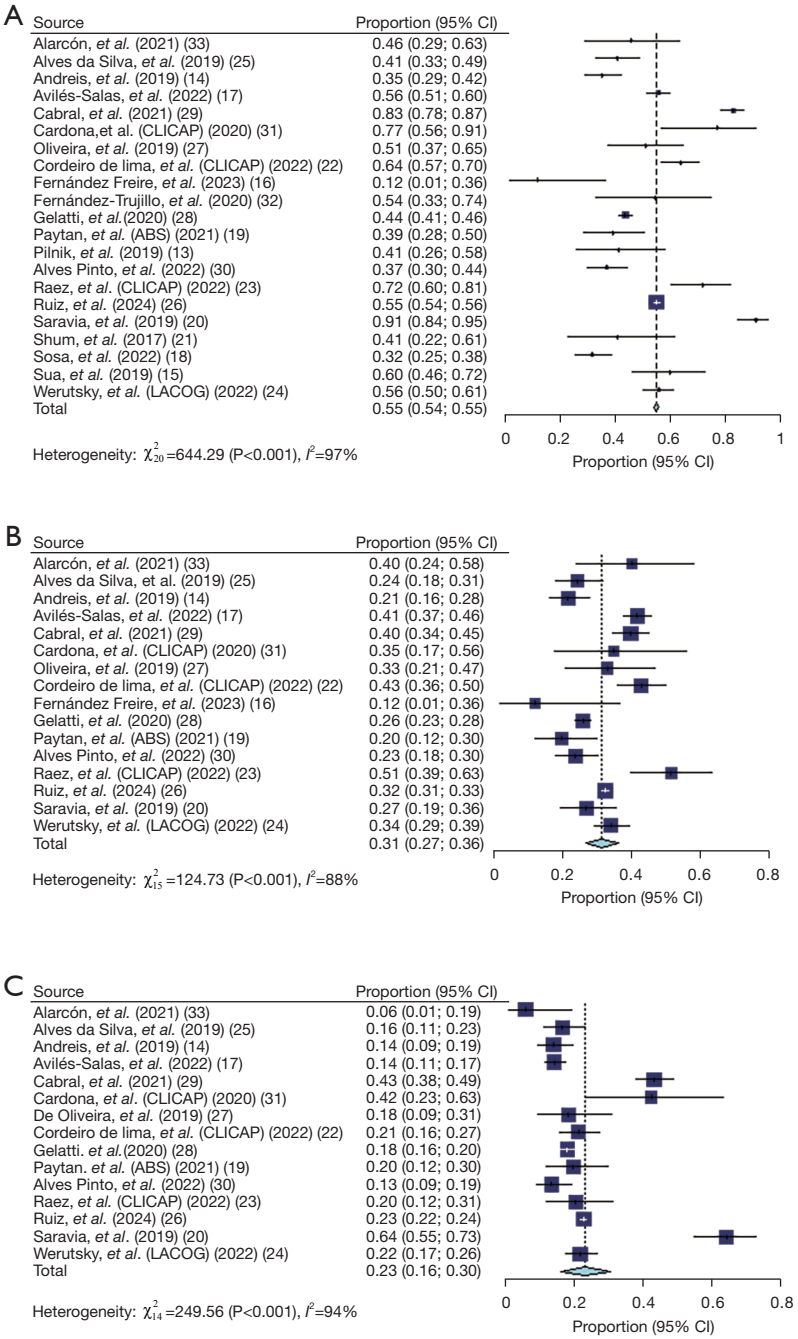

Figure 2 Meta-analysis of PD-L1 expression (13-33). (A) TPS expression ≥1%. (B) TPS expression 1–49%. (C) TPS expression ≥50%. CI, confidence interval; PD-L1, programmed cell death ligand 1; TPS, tumoral proportion score.

molecular alterations was 5.78% (n=250) for patients with positive PD-L1 expression and 3.82% (n=138) for patients with negative PD-L1 expression. The analysis found an association between the PD-L1 expression and ALK positive (OR =1.54; 95% CI: 1.24–1.92).

Quality assessment

We evaluated the quality of 14 out of the 21 articles that were available in full text (Table S2). Bias risk assessment was conducted using two checklists tailored to the design of

cross-sectional and cohort studies. Among the former, eight articles were identified. In the study published by Alarcón *et al.* 2021 (33), details regarding outcome measurement were not provided, and frequencies were measured inaccurately. Additionally, concerns about outcome measurement exist in the study by Cabral 2021 (29). The overall performance was adequate. Regarding analytical longitudinal studies, six cohort articles were reviewed. Overall, there was a lack of clarity in all these studies regarding the identification and control of confounding factors.

Discussion

In this study, the prevalence of PD-L1 expression in NSCLC in H/L patients was evaluated in 13,222 NSCLC patients from different Latin America countries. The prevalence calculated was 55% (95% CI: 0.54–0.55). Similar results were presented in a letter to the editor by Cardona *et al.* (34). They described the PD-L1 expression in 57.9% (95% CI: 55.4–60.5%) of 1,450 NSCLC patients from different Colombian regions. Our results are similar to what was observed in other population. In the EXPRESS study that included 2,368 NSCLC patients, the percentage of patients found with PD-L1 TPS ≥50% and TPS ≥1% respectively were, respectively, 22% and 52% in Europe (Austria, Denmark, Germany, Italy, Spain, Sweden, The Netherlands) (n=415), 22% and 53% in Asia Pacific (Japan, Hong Kong, Korea, Singapore, Taiwan) (n=290), 21% and 47% in the Americas (Argentina, Canada, Colombia) (n=220), and finally 24% and 55% in other countries (Russia, Saudi Arabia, Turkey) (n=139) (35,36).

The prognosis is different for patients receiving PD-1/PD-L1 inhibitor-based therapy. In a meta-analysis that included 1,020 cancer patients from 19 prospective randomized controlled clinical trials, Asian cancer patients were shown to have a significantly improved survival benefit compared to non-Asian for the first time (37). This can be explained by immune system differences among populations. A recent article by Bie *et al.* (38) showed that the composition of tumor-infiltrating lymphocytes (TILs) was quite different between Caucasian and Asian LUAD patients. A higher content of resting mast cells was associated with a better prognosis in Asian patients. Additionally, Caucasian patients with higher immune and estimate scores demonstrated better prognoses (P=0.021, P=0.025). However, Asian patients with higher estimate scores showed a worse prognosis (P=0.024).

In NSCLC, high PD-L1 expression has been associated with male gender, smoking, poor tumor differentiation, large tumor size, presence of lymph node metastasis, *EGFR* wild-type status, and *KRAS* mutations (39). PD-L1 expression is also associated with worse survival (40). In the preset study, the results are similar about the gender, smoking, poor tumor differentiation, and advanced stages (*Table 2*). Our data also found more frequent PD-L1 expression in *EGFR* wild-type status (82.5%) with a OR 1.54 (95% CI: 1.24–1.92) and ALK positive with (OR =1.54; 95% CI: 1.24–1.92).

It has been demonstrated that there is a change in PD-L1 expression among NSCLC subtypes. In a systematic review of 42 articles that evaluated PD-L1 expression in NSCLC subtypes published between 2010 and 2017, the expression in LUSC was found to be higher than LUAD. They found that PD-L1 ≥1% in LUSC was 41.05% (n=743/1,810) versus 34.7% (n=826/2,379) in LUAD. The frequency for PD-L1 1–49% was similar to LUSC (47.9%, n=569/1,189) and LUAD (47.3%, n=712/1,507) while the frequency for PD-L1 ≥50% change in the LUSC (16.1%, n=284/1,766) and LUAD (9.33%, n=179/1,919) (41). In the present review, few articles (13,17,25,27,28,30-32) divided the expression based on the NSCLC subtypes. Gelatti *et al.* (28) found similar results in a multicenter study of a Brazilian population that included 1,512 patients. The frequency for PD-L1 1–49% was 30% in LUSC (n=77) and 23.2% in LUAD (n=185) and PD-L1 ≥50% was 22.05% (n=56) in LUSC and 16.19% (n=129) in LUAD.

The molecular profile in LUSC, in turn, is different than it is in LUSC (42). Cardona *et al.* (31) in 26 Colombian patients with LUSC, a high prevalence of mutations was identified in *TP53* (61.5%), *PIK3CA* (34.6%), *MLL2* (34.6%), *KEAP1* (38.4%), and *NOTCH1* (26.9%). PD-L1 expression levels were categorized as negative in 23.1% of patients, 1% in 38.5%, 2–49% in 26.9%, and ≥50% in 11.5%. Higher PD-L1 expression was significantly associated with *TP53* mutations (P=0.037), and greater PD-L1 expression was related to *PIK3CA* alterations (P=0.05).

There are certain limitations in this study. First, clinical information on patients with PD-L1 expression was not collected in a large percentage of studies. Second, data from some Latin American countries may be limited. Third, PD-L1 expression was not assessed in all NSCLC cases included in the studies. Fourth, many authors were part of different Latin American network consortiums that shared the same patient database across various publications. To address this, we excluded most duplicate articles and selected the one with the highest number of patients with

PD-L1 data. Finally, the results may have been influenced by preanalytical factors (such as time to fixation, fixation duration, and sample processing), IHC platforms, clone selections, inter-observer variability in interpretation, and the age of archival tumor tissue.

Conclusions

In conclusion, this meta-analysis provides a comprehensive overview of PD-L1 expression in NSCLC among the H/L population. Our results in prevalence and clinicopathological features are similar to those of other populations. These findings serve as a foundation for advancing personalized treatment approaches in the realm of NSCLC management, particularly in the context of Latin America and its diverse patient population. It is important to note that other factors besides PD-L1 expression may influence the likelihood and success of immunotherapy treatment. Therefore, studies to identify and describe these factors are suggested.

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Footnote

Reporting Checklist: The authors have completed the PRISMA reporting checklist. Available at https://tlcr.amegroups.com/article/view/10.21037/tlcr-24-223/rc

Peer Review File: Available at https://tlcr.amegroups.com/article/view/10.21037/tlcr-24-223/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tlcr.amegroups.com/article/view/10.21037/tlcr-24-223/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Supplementary

Table S1 Search strategy used in this review

Databases	Terms
LILACS	((carcinoma de pulmón de células no pequeñas) OR (cáncer pulmonar de células no pequeñas) OR (adenocarcinoma) OR (carcinoma de células escamosas) OR (neoplasias pulmonares) OR (cáncer pulmonar)) AND ((hispanoamericanos) OR (hispanos) OR (latinas) OR (latinos)) AND (pd-l1) OR (pd-1) OR (pd-1/pd-l1) OR (proteína de muerte programada 1) OR (proteína pd-1) OR (receptor 1 de muerte celular programada) OR (receptor de muerte celular programada 1) OR (ligando de muerte celular programada 1)
Embase and Medline	#1. 'carcinoma, non-small-cell lung'/exp OR 'carcinoma, non-small-cell lung' OR (('carcinoma,'/exp OR carcinoma,) AND 'non small cell' AND ('lung'/exp OR lung)) #2. ('carcinoma,'/exp OR carcinoma,) AND non AND small AND ('cell'/exp OR cell) AND ('lung'/exp OR lung) #3. 'non small cell lung cancer' #4. 'non small' AND cell AND lung AND cancer #5. nonsmall AND cell AND lung AND cancer #6. 'squamous cell carcinoma' #7. 'adenocarcinoma' #8. 'non small cell lung cancer' #9. 'lung tumor' #10. 'lung cancer' #11. hispanic OR 'south and central america' #12. 'hispanic' #13. 'latin american' #14. #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 #15. #11 OR #12 OR #13 #16. 'pd-l1 test kit' #17. 'pdl1 gene' #18. 'programmed death 1 ligand 1' #19. ligand AND programmed AND 'death ligand 1' #20. 'programmed death 1 receptor' #21. 'programmed cell death protein 1 antibody' #22. 'programmed cell death protein 1 inhibitor' #23. #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 #24. #14 AND #15 AND #23 #25. #14 AND #15 AND #23 AND ([embase]/lim OR [medline]/lim OR [preprint]/lim OR [pubmed-not-medline]/lim)

https://dx.doi.org/10.21037/tlcr-24-223

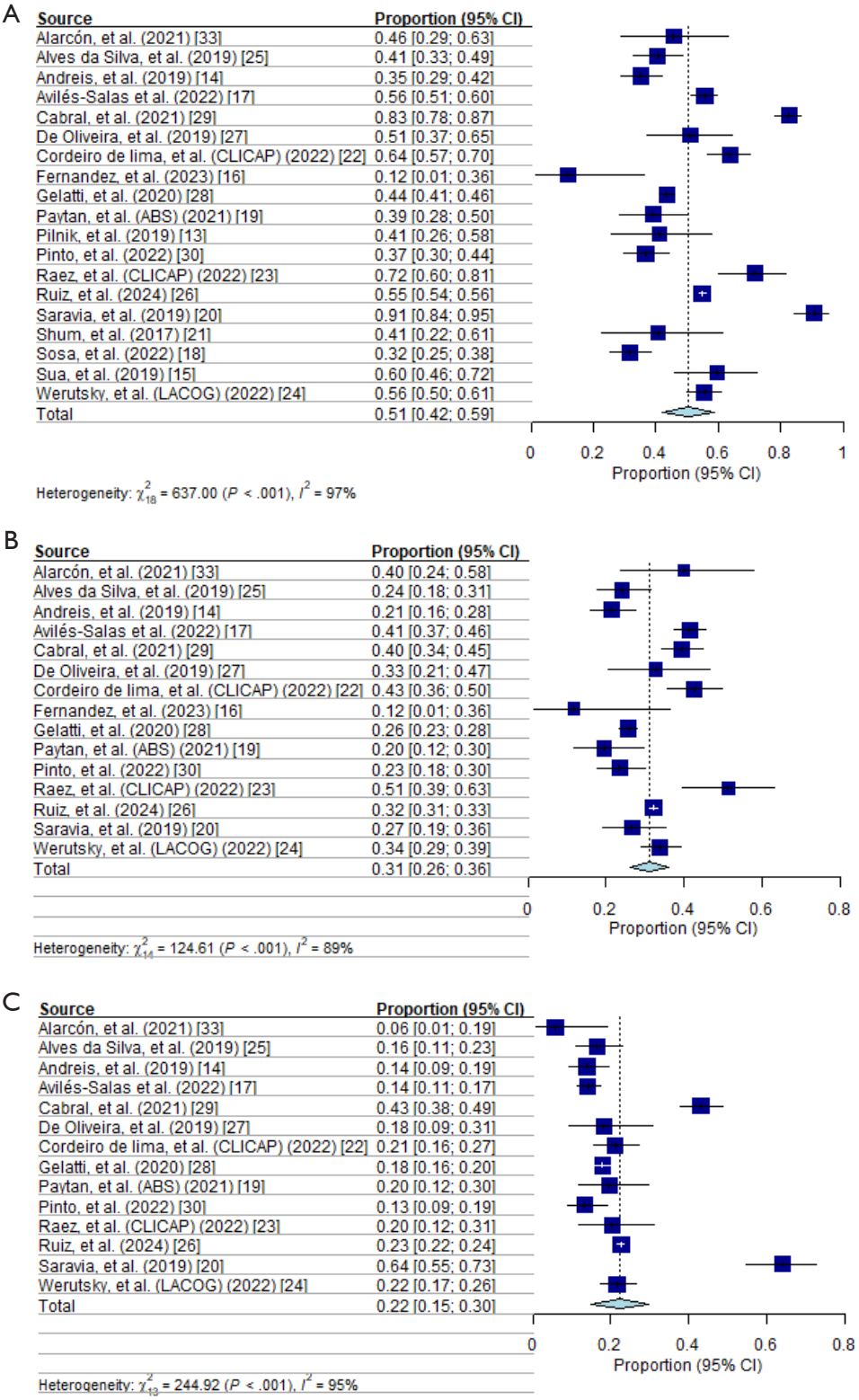

Figure S1 Meta-analysis of PD-L1 expression excluded squamous cell carcinoma. (A) TPS expression ≥1%. (B) TPS expression 1–49%. (C) TPS expression ≥50%. CI, confidence interval; PD-L1, programmed cell death ligand 1; TPS, tumoral proportion score.

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Table S2 Assessment of the quality of evidence and risk of bias for each study using the recommendations of the JBI

Author (ref)	Year	Country	Quality assessment
Pilnik *et al.* (13)	2019	Argentina	Abstract. Quality wasn't assessed
Ruiz *et al.* (26)[§]	2024	Argentina	Meets JBI criteria
Andreis *et al.* (14)[§]	2019	Brazil	Meets JBI criteria
Cabral (29)[§]	2021	Brazil	Outcome measurement concerns
Alves Da Silva *et al.* (25)[§]	2019	Brazil	Meets JBI criteria
Gelatti *et al.* (28)	2020	Brazil	Meets JBI criteria
Oliveira *et al.* (27)[§]	2019	Brazil	Meets JBI criteria
Alves Pinto *et al.* (30)[‡]	2022	Brazil	Meets JBI criteria
Alarcón *et al.* (33)[§]	2021	Colombia	Lack of description in measurement of outcomes and lack of explanation in statistical analysis
Fernández-Trujillo *et al.* (32)[‡]	2020	Colombia	Meets JBI criteria
Cardona *et al.* (31)[‡]	2020	Colombia	Meets JBI criteria
Sua *et al.* (15)	2019	Colombia	Abstract. Quality wasn't assessed
Fernández Freire *et al.* (16)[‡]	2023	Ecuador	Meets JBI criteria
Avilés-Salas *et al.* (17)[§]	2022	Mexico	Meets JBI criteria
Sosa *et al.* (18)	2022	Mexico	Abstract. Quality wasn't assessed
Cordeiro de Lima *et al.* (22)[‡]	2022	Multicentic*	Meets JBI criteria
Raez *et al.* (23)[‡]	2022	Multicentic**	Meets JBI criteria
Werutsky *et al.* (24)	2022	Multicentric***	Abstract. Quality wasn't assessed
Paytan *et al.* (19)	2021	Peru	Abstract. Quality wasn't assessed
Shum *et al.* (21)	2017	USA	Abstract. Quality wasn't assessed
Saravia *et al.* (20)	2019	USA	Abstract. Quality wasn't assessed

[§], cross sectional studies; [‡], longitudinal studies; *, multicentric: Mexico, Colombia, Costa Rica, Argentina, Chile, Peru, Brazil , H/L in US; **, multicentric: H/L in US, Mexico, Colombia; ***, multicentric: Argentina, Brazil, Colombia , Mexico. JBI, Joanna Briggs Institute; H/L, Hispanic/Latino.

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