

# Prevalence and associated factors of diabetic retinopathy in Latin American countries: a scoping review

Prevalência e fatores associados à retinopatia diabética em países da América Latina: uma revisão de escopo

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## ABSTRACT

**Objective:** To gather the available evidence in the literature on the prevalence and associated factors of diabetic retinopathy (DR) in Latin America.

**Methods:** This scoping review was developed according to the PRISMA-ScR. Prevalence data were summarized by weighted mean, considering the type of DM and country. For the analysis of associated factors, meta-analyses were performed with the most homogeneous studies, and the ORs and their 95% CIs were calculated.

**Results:** Forty-two articles published between 2004 and 2020 were included in this study. The mean prevalence of DR ranged from 15.0% in Costa Rica to 32.7% in Brazil.

**Conclusion:** This variation may be related to the diagnostic method, age of the studied population, duration of disease, glycemic control, or other associated factors such as the presence of diabetic nephropathy or hypertension. This review discloses an important burden of DR in Latin America and highlights the need for further in-country studies.

## RESUMO

**Objetivo:** O objetivo desta revisão foi reunir as evidências disponíveis na literatura sobre a prevalência e os fatores associados à retinopatia diabética na América Latina.

**Métodos:** Esta é uma revisão de escopo desenvolvida de acordo com o PRISMA-ScR. Os dados de prevalência foram resumidos por escopo ponderada, considerando o tipo de diabetes mellitus e o país. Para a análise dos fatores associados, foram realizadas metanálises com os estudos mais homogêneos e calculados as razões de chance e seus intervalos de confiança de 95%.

**Resultados:** Foram publicados 42 artigos entre 2004 e 2020, os quais foram incluídos neste estudo. A prevalência média de retinopatia diabética variou de 15,0%, na Costa Rica, a 32,7%, no Brasil.

**Conclusão:** Essa variação pode estar relacionada ao método de diagnóstico, à idade da população estudada, à duração da doença, ao controle glicêmico ou a outros fatores associados, como a presença de nefropatia diabética ou hipertensão. Esta revisão revelou um ônus importante da retinopatia diabética na América Latina e destaca a necessidade de mais estudos nos países.

## INTRODUCTION

The prevalence of diabetes mellitus (DM) has been increasing worldwide, raising the risk of its complications. Chronic hyperglycemia may result in lesions to several organs, compromising the quality of life, high health costs, and increased mortality. Among the various modifications diabetes can cause to the ocular tissues, the best known and with the greatest potential for vision impairment is diabetic retinopathy (DR), the leading cause of blindness in economically active people. Retinopathy results from complex inflammatory and immunological phenomena that lead to injury to the small vessels of the retina.<sup>(1,2)</sup>

The prevalence of DR varies among studies and regions of the world. According to the International Agency for the Prevention of Blindness (IAPB) Vision Atlas, 103 million people worldwide (22.3% of those living with DM) have some degree of DR.<sup>(3)</sup> The Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR) found a 17% prevalence of DR after 5 years and 98% after 15 years of DM diagnosis in people who were diagnosed under 30 years old and 29% and 78%, respectively, in those diagnosed over 30 years old.<sup>(4)</sup>

Early detection and treatment can prevent the progression of retinopathy and visual disability. Treatment varies according to the severity of retinopathy and may prevent severe visual loss in up to 90% of the cases.<sup>(2,5)</sup>

Despite the increasing prevalence of DM all over the world, the rates of visual impairment caused by DR can be reduced through early detection and adequate glyce-mic control. Even if there are currently effective screening mechanisms and treatment options for DR, these services are not evenly distributed across populations, and population data recording may be scarcer in developing countries. Thus, this scoping review aims to gather the available evidence in the literature about DR prevalence and associated factors in Latin American countries.

## METHODS

This scoping review protocol was developed according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR)<sup>(6)</sup> and has been registered at Open Science Framework (<https://osf.io/7rdyj/>).

Observational studies published in Latin American countries between the years 2000 to 2021, in Portuguese, English, or Spanish languages, whose participants were adults diagnosed with type 1 or II DM, and that evaluated prevalence and/or risk factors for DR were included. The

exclusion criteria were studies that addressed non-modifiable risk factors (genetic/biochemical) of DR, those whose participants were only patients already diagnosed with DR, clinical studies, animal studies, and review articles.

Searches were performed in MEDLINE®/PubMed®, Brazilian Virtual Health Library (VHL), and Embase databases in January 2021 through a comprehensive title and abstract search conducted by independent researchers.

The search descriptors were used according to standards defined by each information source – Medical Subject Headings (MeSH), from MEDLINE®; Health Sciences Descriptors (DeCS, from the website in Brazilian Portuguese *Descritores em Ciências da Saúde*) from VHL; Emtree, from Embase. These terms were combined using the Boolean operators “and” and “or”. The operator “not” was not used. (Table 1)

**Table 1.** Search strategy by literature base

Bibliographic base	Search strategy
MEDLINE®/PubMed®	("Diabetic Retinopathy") AND ("Americas" OR "Latin America" OR "South America" OR "Central America" OR "Mexico" OR "Brazil") AND ("Prevalence" OR "Risk Factors" OR "incidence" OR "morbidity" OR "mortality" OR "epidemiology")
VHL	(diabetic retinopathy) AND ("Prevalence" OR "Risk Factors" OR "incidence" OR "morbidity" OR "mortality" OR "epidemiology")
EMBASE	#1 'diabetic retinopathy'; ab,ti AND [2000-2021]/py #2 ('western hemisphere':ab,ti OR south:ab,ti) AND 'central america':ab,ti OR mexico:ab,ti OR brazil:ab,ti #3 (prevalence:ab,ti OR 'risk factor':ab,ti OR incidence:ab,ti OR morbidity:ab,ti OR epidemiology:ab,ti) AND [2000-2021]/py #4 #1 AND #2 AND #3

VHL: Virtual Health Library.

After excluding duplicate papers, the remaining titles and abstracts were independently peer-reviewed by four reviewers to identify articles potentially eligible for a full reading. The qualitative synthesis included those studies that met all inclusion criteria. The Kappa concordance index was calculated at the end of the selection. In cases of disagreement, a consensus was reached through discussion among reviewers.

Two reviewers independently extracted data from included studies using a predefined form, containing: first author, year of publication, study design (cohort or cross-sectional), country studied, sample size, mean age, race, sex (male or female), DM classification (DM 1 or DM 2), the observed prevalence in percentage and confidence interval (95%CI), definition of a significant risk factor with odds ratio (OR)/relative risk (RR), 95%CI and p-value.

The prevalence rates extracted from included articles were synthesized using the weighted mean, considering the type of DM and country of study. For this analysis, outliers were excluded due to high heterogeneity among studies.

Forest plots were used to assess pooled estimates and corresponding 95% confidence intervals with inverse-variance weights obtained from a visually random-effects model. The Cochran Q test (significance level of  $p < 0.10$ ) and the I<sup>2</sup> statistic were calculated to assess heterogeneity.

Furthermore, meta-analyses to assess risk factors for DR were also conducted. For these analyses, ORs and their respective 95% CIs were calculated following the random-effects model due to heterogeneity among studies ( $p < 0.10$ ;  $I^2 > 50\%$ ).

For all meta-analyses, subgroup analyses by type of study (cross-sectional and cohort) and type of DM were performed to create more homogeneous groups. A meta-regression analysis was conducted to explore potential sources of heterogeneity for DM 2 (Table 2), including the sample size, year of study (before 2010; 2010 ahead), country (Brazil; Chile; Colombia; Costa Rica; Mexico; Peru), and study design (cohort; cross-sectional). In all analyses, a p-value  $< 0.05$  was considered statistically significant. Stata software, version 15.0 (Stata Corporation, College Station, USA) was used for data analysis.

**Table 2.** Meta-regression analysis to potential sources of heterogeneity for diabetes mellitus 2

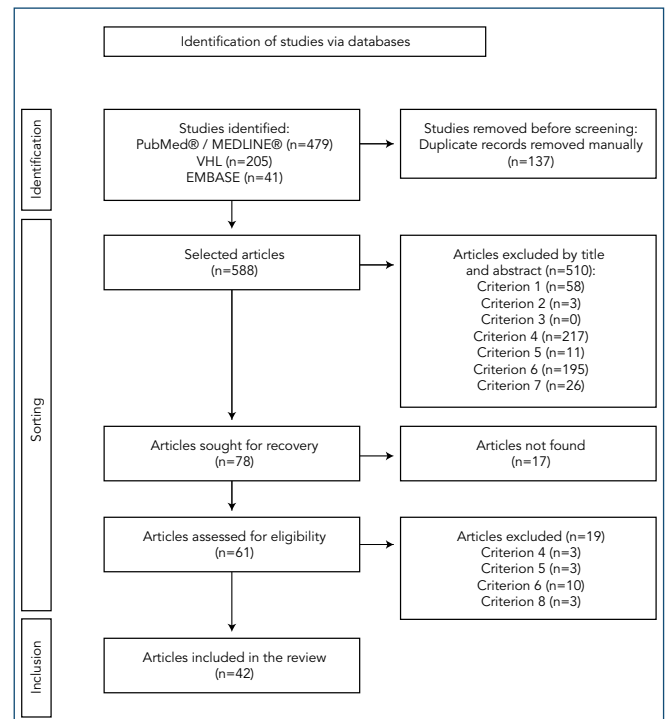
Subgroup	Number of studies	Estimate	95%CI	p-value
Sample size	18	-0.0001	-0.0002--0.0001	0.023
Year				
Before 2010	5	-	-	-
From 2010	13	-0.1469	-0.2604--0.0334	0.011
Country				
Brazil	10	-	-	-
Chile	1	-0.2340	-0.4016--0.0663	0.006
Colombia	1	0.0838	-0.1329-0.3005	0.449
Costa Rica	1	-0.1244	-0.2517-0.0029	0.055
Mexico	3	-0.1416	-0.2504--0.0328	0.011
Peru	2	-0.0389	-0.1625-0.0847	0.538
Study design				
Cohort	5	-	-	-
Cross-sectional	13	0.0291	-0.0463-0.1045	0.449
Residual heterogeneity				
I <sup>2</sup>			57.0%	
p-value			<0.001	
R <sup>2</sup>			88.0%	

95%CI: 95% of confidence interval.

## RESULTS

A total of 725 articles were found in the three databases, and 137 were excluded for being duplicates. Of these, 78 were evaluated as eligible and submitted to a full reading, and 17 were not found. In cases of divergence, the decision about including or not the articles were based on consensus among researchers, resulting in 42 articles being included in the review. The Kappa concordance index

was 0.891 (95%CI 0.827-0.954). All papers provided information about the prevalence of RD and nine also explored risk factors for RD. The study selection process was summarized, according to PRISMA guidelines in Figure 1.



VHL: Virtual Health Library.

**Figure 1.** Flowchart of article selection

Inclusion criteria: (1) Type: observational studies; (2) Period: 2000 to 2021; (3) Language: Portuguese, English, and Spanish; (4) Region: Latin American countries; (5) Participants: Adults diagnosed with DM type 1 or 2; (6) Outcome: to assess the prevalence and/or risk factors for DR. Exclusion criteria: (7) Address only non-modifiable (genetic/biochemical) risk factors for DR; (8) Studies that included only participants with a previous diagnosis of DR.

Forty-two articles published between 2004 and 2020 were included in this study (Table 3), 23 from Brazil, 8 from Mexico, 4 from Chile, 2 from Peru, and 1 from Colombia, Costa Rica, Ecuador, Puerto Rico, and Venezuela. Among the studies included, 76.2% were cross-sectional and 23.8% were cohort studies. As for the division by type of DM, 16 studies included only patients with type 2 DM, and 8 included only patients with type 1 DM. Two studies addressed both populations, so one was included in the analysis for both types of DM and the other only for type 2 DM - the proportion of DMI participants was less than 1.0% (Table 4). Three articles were excluded from the analysis due to the high heterogeneity of results. The remaining studies ( $n = 13$ ) worked with both types of DM and did not present their results separately.

**Table 3.** Selected articles (7-48)

Order	Author	Country	Year	Title	DOI
1	Abuauad S, et al. <sup>(7)</sup>	Chile	2014	Prevalence of diabetic retinopathy and macular edema in the diabetic population of CESFAM Cordillera Andina de Los Andes	<a href="https://doi.org/10.5354/0719-5281.2014.30759">https://doi.org/10.5354/0719-5281.2014.30759</a>
2	Adriánzén RE, et al. <sup>(8)</sup>	Peru	2019	Frequency and severity of diabetic retinopathy in patients with type 2 diabetes mellitus at the Institute Regional de Oftalmología.	<a href="http://dx.doi.org/10.17843/rpmesp.2019.362.4076">http://dx.doi.org/10.17843/rpmesp.2019.362.4076</a>
3	Almeida FK, et al. <sup>(9)</sup>	Brazil	2011	Microvascular Complications and Cardiac Autonomic Dysfunction in Patients with Type 1 Diabetes Mellitus	<a href="https://doi.org/10.1590/S0066-782X2011005000047">https://doi.org/10.1590/S0066-782X2011005000047</a>
4	Barriá von-B, et al. <sup>(10)</sup>	Chile	2014	Análisis de los pacientes con diabetes controlados a nivel primaria en el Servicio de Salud Concepción	<a href="https://pesquisa.bvsalud.org/portal/resource/pt/lil-779318">https://pesquisa.bvsalud.org/portal/resource/pt/lil-779318</a>
5	Cardoso CRL, et al. <sup>(11)</sup>	Brazil	2008	Predictors of development and progression of microvascular complications in a cohort of Brazilian type 2 diabetic patients	<a href="http://dx.doi.org/10.1016/j.jdiacomp.2007.02.004">http://dx.doi.org/10.1016/j.jdiacomp.2007.02.004</a>
6	Cardoso CRL, et al. <sup>(12)</sup>	Brazil	2017	Predictors of Development and Progression of Retinopathy in Patients with Type 2 Diabetes: Importance of Blood Pressure Parameters	<a href="http://dx.doi.org/10.1038/s41598-017-05159-6">http://dx.doi.org/10.1038/s41598-017-05159-6</a>
7	Cardoso CRL, et al. <sup>(13)</sup>	Brazil	2018	Long-term visit-to-visit glycemic variability as predictor of micro- and macrovascular complications in patients with type 2 diabetes: The Rio de Janeiro Type 2 Diabetes Cohort Study	<a href="https://doi.org/10.1186/s12933-018-0677-0">https://doi.org/10.1186/s12933-018-0677-0</a>
8	Cardoso CRL, et al. <sup>(14)</sup>	Brazil	2019	Prognostic impact of carotid intima-media thickness and carotid plaques on the development of micro and macrovascular complications in individuals with type 2 diabetes: the Rio de Janeiro type 2 diabetes cohort study	<a href="https://doi.org/10.1186/s12933-019-0809-1">https://doi.org/10.1186/s12933-019-0809-1</a>
9	Cardoso CRL, et al. <sup>(15)</sup>	Brazil	2020	Prognostic importance of visit-to-visit blood pressure variability for micro and macrovascular outcomes in patients with type 2 diabetes: The Rio de Janeiro Type 2 Diabetes Cohort Study	<a href="https://doi.org/10.1186/s12933-020-01030-7">https://doi.org/10.1186/s12933-020-01030-7</a>
10	Cervantes-Castañeda RA, et al. <sup>(14)</sup>	Mexico	2014	Deficient prevention and late treatment of diabetic retinopathy in Mexico	<a href="https://pubmed.ncbi.nlm.nih.gov/25375282/">https://pubmed.ncbi.nlm.nih.gov/25375282/</a>
11	Chacon DA, et al. <sup>(17)</sup>	Brazil	2005	Funduscopy findings and alterations in the diabetic foot in patients at Onofre Lopes University Hospital/UFRN	<a href="https://doi.org/10.1590/S0102-86502005000700002">https://doi.org/10.1590/S0102-86502005000700002</a>
12	Drummond KRG, et al. <sup>(18)</sup>	Brazil	2018	Regional differences in the prevalence of diabetic retinopathy: a multi-center study in Brazil	<a href="https://doi.org/10.1186/s13098-018-0319-4">https://doi.org/10.1186/s13098-018-0319-4</a>
13	Escarião PHG, et al. <sup>(19)</sup>	Brazil	2008	Epidemiology and regional differences in retinopathy diabetics in Pernambuco, Brazil	<a href="https://doi.org/10.1590/S0004-27492008000200008">https://doi.org/10.1590/S0004-27492008000200008</a>
14	Espinoza AG, et al. <sup>(20)</sup>	Ecuador	2006	World day of vision: campaign against blindness by diabetic retinopathy. October 2004, Guayaquil - Ecuador	<a href="https://editorial.ucsg.edu.ec/ojs-medicina/index.php/ucsg-medicina/article/view/282">https://editorial.ucsg.edu.ec/ojs-medicina/index.php/ucsg-medicina/article/view/282</a>
15	Esteves JF, et al. <sup>(21)</sup>	Brazil	2009	Prevalence of diabetic retinopathy in patients with type 1 diabetes mellitus	<a href="https://doi.org/10.1590/S0104-42302009000300017">https://doi.org/10.1590/S0104-42302009000300017</a>
16	García-Alcolea EE, et al. <sup>(22)</sup>	Venezuela	2009	Clinical behavior of diabetic retinopathy in Parroquia Maiquetía, Vargas, Venezuela 2007	<a href="https://www.medigraphic.com/cgi-bin/new/resumen.cgi?IDARTICULO=20519">https://www.medigraphic.com/cgi-bin/new/resumen.cgi?IDARTICULO=20519</a>
17	Gerchman F, et al. <sup>(23)</sup>	Brazil	2008	Vascular complications of black patients with type 2 diabetes mellitus in Southern Brazil	<a href="https://doi.org/10.1590/S0100-879X2008005000034">https://doi.org/10.1590/S0100-879X2008005000034</a>
18	Gomes MB, et al. <sup>(24)</sup>	Brazil	2019	Relationship between health care insurance status, social determinants and prevalence of diabetes-related microvascular complications in patients with type 1 diabetes: a nationwide survey in Brazil	<a href="https://doi.org/10.1007/s00592-019-01308-7">https://doi.org/10.1007/s00592-019-01308-7</a>
19	Jiménez-Báez MV, et al. <sup>(25)</sup>	Mexico	2015	Early diagnosis of diabetic retinopathy in primary care	<a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4437282/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4437282/</a>
20	Jost BS, et al. <sup>(26)</sup>	Brazil	2010	Prevalence of diabetic retinopathy in the population with type 2 diabetes mellitus in the city of Luzerna - SC	<a href="https://doi.org/10.1590/S0004-27492010000300010">https://doi.org/10.1590/S0004-27492010000300010</a>
21	Lima-Gómez V, et al. <sup>(27)</sup>	Mexico	2004	Crystal opacity in diabetics. Prevalence and association with visual impairment and retinopathy	<a href="https://www.medigraphic.com/cgi-bin/new/resumen.cgi?IDARTICULO=280">https://www.medigraphic.com/cgi-bin/new/resumen.cgi?IDARTICULO=280</a>
22	Lopez-Ramos A, et al. <sup>(28)</sup>	Mexico	2018	Rapid assessment of avoidable blindness: Prevalence of blindness, visual impairment and diabetes in nuevo leon, Mexico 2014	<a href="https://doi.org/10.1080/09286586.2018.1501498">https://doi.org/10.1080/09286586.2018.1501498</a>
23	Lopez-Star EM, et al. <sup>(29)</sup>	Mexico	2018	Rapid assessment of avoidable blindness including diabetic retinopathy in Queretaro, Mexico	<a href="http://dx.doi.org/10.24875/RMOE.M18000005">http://dx.doi.org/10.24875/RMOE.M18000005</a>
24	Martínez J, et al. <sup>(30)</sup>	Costa Rica	2011	Diabetic retinopathy screening using single-field digital fundus photography at a district level in Costa Rica: a pilot study	<a href="http://dx.doi.org/10.1007/s10792-010-9413-9">http://dx.doi.org/10.1007/s10792-010-9413-9</a>
25	Melo LGN, et al. <sup>(31)</sup>	Brazil	2018	Current epidemiology of diabetic retinopathy in patients with type 1 diabetes: a national multicenter study in Brazil	<a href="https://doi.org/10.1186/s12889-018-5859-x">https://doi.org/10.1186/s12889-018-5859-x</a>
26	Mendoza-Herrera K, et al. <sup>(32)</sup>	Mexico	2017	A Diabetic Retinopathy Screening Tool for Low-Income Adults in Mexico	<a href="https://doi.org/10.5888/pcd14.170157">https://doi.org/10.5888/pcd14.170157</a>
27	Pedrosa DR, et al. <sup>(33)</sup>	Brazil	2013	Prevalence of diabetic retinopathy in patients seen by the Health Care Strategy Family Health in the municipality of Ananindeua - PA	<a href="http://dx.doi.org/10.5712/rbmf7(23)394">http://dx.doi.org/10.5712/rbmf7(23)394</a>
28	Perrasse AV, et al. <sup>(34)</sup>	Colombia	2006	The control of diabetes mellitus and its complications in Medellín, Colombia, 2001-2003	<a href="https://www.scielosp.org/article/rpsp/2006.v20n6/393-402/">https://www.scielosp.org/article/rpsp/2006.v20n6/393-402/</a>
29	Polack S, et al. <sup>(35)</sup>	Mexico	2012	Rapid Assessment of Avoidable Blindness and Diabetic Retinopathy in Chiapas, Mexico	<a href="https://doi.org/10.1016/j.ophtha.2011.11.002">https://doi.org/10.1016/j.ophtha.2011.11.002</a>
30	Rodrigues TC, et al. <sup>(36)</sup>	Brazil	2010.1	Masked hypertension, nocturnal blood pressure and retinopathy in normotensive patients with type 1 diabetes	<a href="http://dx.doi.org/10.1016/j.diabres.2009.10.016">http://dx.doi.org/10.1016/j.diabres.2009.10.016</a>
31	Rodrigues TC, et al. <sup>(37)</sup>	Brazil	2010.2	Characterization of patients with type 1 diabetes mellitus in southern Brazil: chronic complications and associated factors	<a href="https://doi.org/10.1590/S0104-42302010000100019">https://doi.org/10.1590/S0104-42302010000100019</a>
32	Rodríguez ME, et al. <sup>(38)</sup>	Chile	2011	Prevalence of diabetic retinopathy in dependent inhabitants of the Western Metropolitan Health Service (SSMOC)	<a href="http://bases.bireme.br/cgi-bin/wxislind.exe/iah/online/?IsisScript=iah/iah.xis&amp;src=google&amp;base=LILACS&amp;lang=p&amp;nextAction=lnk&amp;exprSearch=609944&amp;indexSearch=ID">http://bases.bireme.br/cgi-bin/wxislind.exe/iah/online/?IsisScript=iah/iah.xis&amp;src=google&amp;base=LILACS&amp;lang=p&amp;nextAction=lnk&amp;exprSearch=609944&amp;indexSearch=ID</a>
33	Rodríguez NM, et al. <sup>(39)</sup>	Puerto Rico	2016	Prevalence of Diabetic Retinopathy in a Clinic Population from Puerto Rico	<a href="http://dx.doi.org/10.4088/16/9307-0750/0">http://dx.doi.org/10.4088/16/9307-0750/0</a>
34	Rosa LCGFD, et al. <sup>(40)</sup>	Brazil	2019	HbA1c variability and long-term glycemic control are linked to diabetic retinopathy and glomerular filtration rate in patients with type 1 diabetes and multiethnic background	<a href="https://doi.org/10.1016/j.jdiacomp.2019.05.022">https://doi.org/10.1016/j.jdiacomp.2019.05.022</a>

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Order	Author	Country	Year	Title	DOI
35	Sabag-Ruiz E, et al. <sup>(41)</sup>	Mexico	2006	Chronic complications in diabetes mellitus. Prevalence in a medical unit family	<a href="https://www.medigraphic.com/cgi-bin/new/resumen.cgi?IDARTICULO=9182">https://www.medigraphic.com/cgi-bin/new/resumen.cgi?IDARTICULO=9182</a>
36	Sampaio E, et al. <sup>(42)</sup>	Brazil	2007	Nephropathy and Retinopathy in Type 1 Diabetics from a University Multiprofessional Care Program	<a href="https://doi.org/10.1590/S0004-27302007000300008">https://doi.org/10.1590/S0004-27302007000300008</a>
37	Santos KG, et al. <sup>(43)</sup>	Brazil	2005	Prevalence of retinopathy in Caucasians type 2 diabetic patients from the South of Brazil and relationship with clinical and metabolic factors	<a href="https://doi.org/10.1590/S0100-879X2005000200010">https://doi.org/10.1590/S0100-879X2005000200010</a>
38	Schellini SA, et al. <sup>(44)</sup>	Brazil	2014	Prevalence of Diabetes and Diabetic Retinopathy in a Brazilian Population	<a href="https://doi.org/10.3109/09286586.2013.868004">https://doi.org/10.3109/09286586.2013.868004</a>
39	Souza EV, et al. <sup>(45)</sup>	Brazil	2004	Diabetic Retinopathy in Patients of a multidisciplinary care at the Hospital das Clínicas de Ribeirão Preto - USP	<a href="https://doi.org/10.1590/S0004-27492004000300012">https://doi.org/10.1590/S0004-27492004000300012</a>
40	Tres GS, et al. <sup>(46)</sup>	Brazil	2007	Prevalence and Characteristics of Diabetic Polyneuropathy in Passo Fundo, South of Brazil	<a href="https://doi.org/10.1590/S0004-27302007000600014">https://doi.org/10.1590/S0004-27302007000600014</a>
41	Verdaguer J, et al. <sup>(47)</sup>	Chile	2009	Natural history of retinopathy diabética en un estudio a largo plazo en pacientes con diabetes tipo 1. Risk factors for progression to proliferative disease	<a href="http://dx.doi.org/10.4067/S0034-98872009000900002">http://dx.doi.org/10.4067/S0034-98872009000900002</a>
42	Villena JE, et al. <sup>(48)</sup>	Peru	2011	Prevalence of diabetic retinopathy in Peruvian patients with type 2 diabetes: results of a hospital-based retinal telescreening program	<a href="https://www.scielosp.org/pdf/rpsp/2011.v30n5/408-414/en">https://www.scielosp.org/pdf/rpsp/2011.v30n5/408-414/en</a>

**Table 4.** Characteristics of the studies, by type of diabetes

Author	Country	Year	Study design	DM Type	Sample (n)	Average age	Gender – male (%)	RD prevalence (%)
Perrasse AV, et al. <sup>(34)</sup>	Colombia	2006	Transversal	DM 1	123	-	-	31.7
Sampaio E, et al. <sup>(42)</sup>	Brazil	2007	Transversal	DM 1	81	26.4	35.5	21.0
Esteves JF, et al. <sup>(21)</sup>	Brazil	2009	Transversal	DM 1	437	-	50.3	44.4
Verdaguer J, et al. <sup>(47)†</sup>	Chile	2009	Cohort	DM 1	39	46.5	48.7	92.3
Rodrigues TC, et al. <sup>(36)</sup>	Brazil	2010	Transversal	DM 1	103	-	29.2	35.9
Rodrigues TC, et al. <sup>(37)</sup>	Brazil	2010	Transversal	DM 1	533	33.0	50.5	43.3
Almeida FK, et al. <sup>(9)</sup>	Brazil	2011	Transversal	DM 1	81	40.5	54.3	54.4
Drummond KRG, et al. <sup>(18)</sup>	Brazil	2018	Transversal	DM 1	1,760	30.2	43.9	33.0
Melo LGN, et al. <sup>(31)</sup>	Brazil	2018	Transversal	DM 1	1,644	30.1	44.2	35.7
Gomes MB, et al. <sup>(24)</sup>	Brazil	2019	Transversal	DM 1	1,760	29.9	44.1	35.8
Rosa LCGFD, et al. <sup>(40)†</sup>	Brazil	2019	Cohort	DM 1	220	29.6	40.0	18.0
Lima-Gómez V, et al. <sup>(27)</sup>	Mexico	2004	Transversal	DM 2	313	58.5	33.0	18.8
Santos KG, et al. <sup>(43)</sup>	Brazil	2005	Cohort	DM 2	210	58.7	32.4	47.1
Perrasse AV, et al. <sup>(34)</sup>	Colombia	2006	Transversal	DM 2	2,854	-	-	31.9
Tres GS, et al. <sup>(46)</sup>	Brazil	2007	Transversal	DM 2	340	57.8	40.0	28.8
Cardoso CRL, et al. <sup>(15)</sup>	Brazil	2008	Cohort	DM 2	471	60.5	65.8	22.5
Gerchman F, et al. <sup>(23)</sup>	Brazil	2008	Transversal	DM 2	1,810	-	46.8	21.5
Jost BS, et al. <sup>(26)</sup>	Brazil	2010	Transversal	DM 2	120	63.5	48.3	38.4
Martínez J, et al. <sup>(30)‡</sup>	Costa Rica	2011	Transversal	DM 2	1,319	60.5	39.8	21.9
Villena JE, et al. <sup>(48)</sup>	Peru	2011	Transversal	DM 2	1,222	59.0	-	23.1
Pedrosa DR, et al. <sup>(33)</sup>	Brazil	2013	Transversal	DM 2	40	58.1	35.5	40.7
Abuauad S, et al. <sup>(7)</sup>	Chile	2014	Transversal	DM 2	468	-	39.1	24.8
Schellini SA, et al. <sup>(44)†</sup>	Brazil	2014	Transversal	DM 2	407	58.8	33.4	7.62
Jiménez-Báez MV, et al. <sup>(25)</sup>	Mexico	2015	Transversal	DM 2	105	-	44.8	23.8
Cardoso CRL, et al. <sup>(12)</sup>	Brazil	2017	Cohort	DM 2	544	60.2	37.1	26.5
Mendoza-Herrera K, et al. <sup>(32)</sup>	Mexico	2017	Transversal	DM 2	1,000	57.2	27.0	31.7
Cardoso CRL, et al. <sup>(11)</sup>	Brazil	2018	Cohort	DM 2	654	60.1	38.0	32.7
Adriánzén RE, et al. <sup>(8)</sup>	Peru	2019	Transversal	DM 2	3,239	59.0	37.3	25.9
Cardoso CRL, et al. <sup>(14)</sup>	Brazil	2019	Cohort	DM 2	478	60.0	36.0	33.5
Cardoso CRL, et al. <sup>(13)</sup>	Brazil	2020	Cohort	DM 2	632	60.0	38.6	32.4

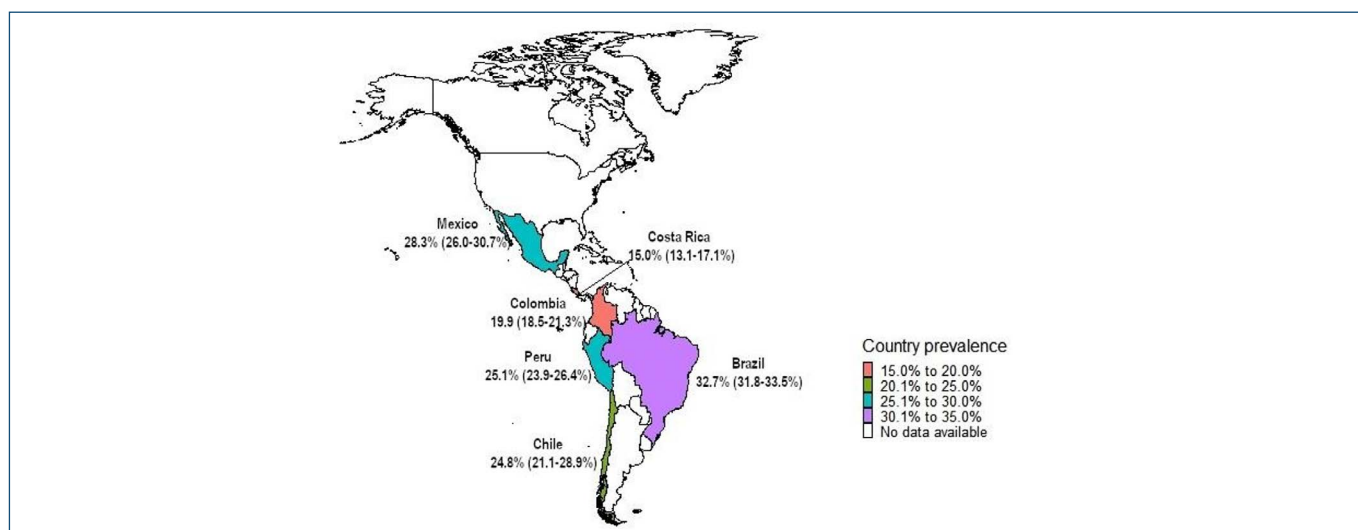
\* Includes data for DM type 1 and type 2; † Studies did not make up the prevalence analysis given the high heterogeneity; ‡ Includes data for both types of DM, with the proportion for type 1 DM being less than 1.0%.  
DM: diabetes mellitus RD: diabetic retinopathy.

The overall prevalence of DR ranged from 15.0% (95%CI 13.1-17.1%) in Costa Rica to 32.7% (95%CI 31.8-33.5%) in Brazil (Figure 2).

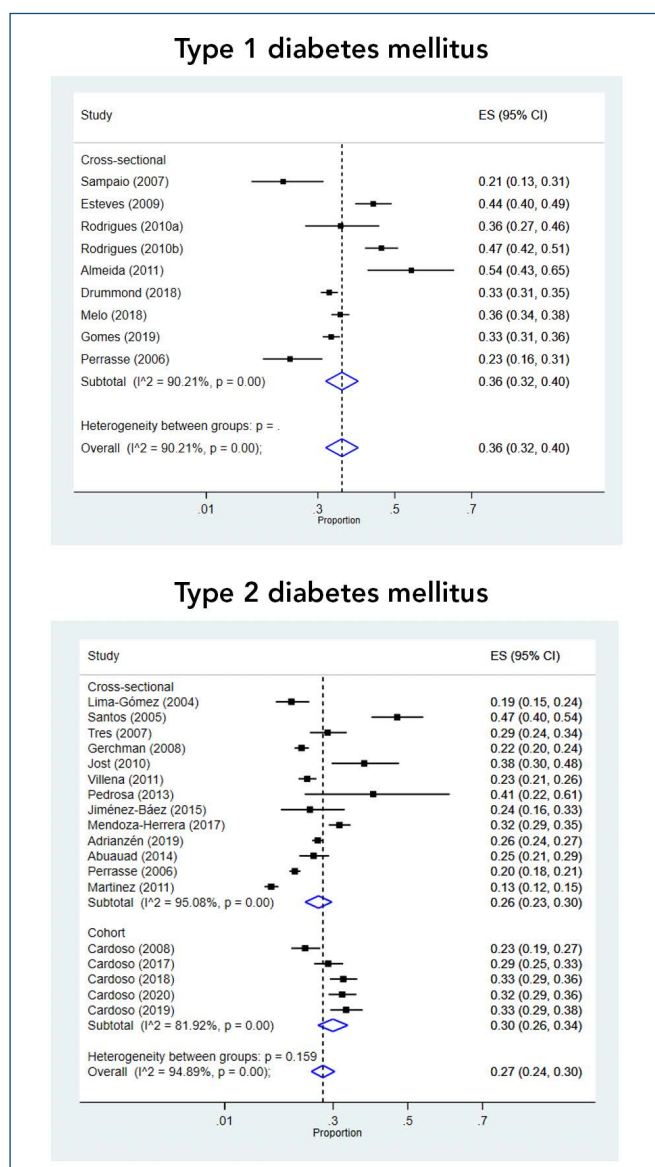
Regarding type, 1 DM, the mean age of patients already diagnosed with DR ranged from 26.4 to 40.5 years. Moreover, the proportion of male patients ranged from 29.2% to 54.3%. The prevalence of DR observed in the population with type 1 DM ranged from 21.0% to 54.4%, maintaining a mean of 36.0% (95%CI 32.0-40.0%). Both

prevalence extremes were identified in Brazilian studies (Figure 3). Meta-regression analysis for DM 2 showed that the sample size, year of study, and country were the sources of heterogeneity. The regression explained the majority of sources of heterogeneity (Adj R-squared=88.0%) (Table 1).

As for the population with type 2 DM, the mean age ranged from 57.2 to 63.5 years. Only one study had a male majority, with 65.8% of the participants. The prevalence



**Figure 2.** Mean prevalence of diabetic retinopathy in Latin American countries.



**Figure 3.** Prevalence of diabetic retinopathy, by type of diabetes mellitus and type of study.

of DR in this group ranged from 18.8% in Mexico to 47.1% in Brazil, with a mean of 27.0% (95%CI 24.0-30.0%) (Figure 3).

The analysis regarding the risk factors related to the presence of DR showed that in patients with type 1 diabetes, the following factors stood out: duration of diabetes, presence of arterial hypertension, increased glycated hemoglobin, presence of diabetic nephropathy, and increased age. In type 2 diabetes, an association was found concerning the following factors: duration of diabetes, increased glycated hemoglobin, and presence of diabetic nephropathy (Table 5).

Patients living longer with DM have higher odds of developing DR when compared to people with a shorter disease duration (OR 1.08; 95%CI 1.06-1.10; p = 0.134, I<sup>2</sup> = 46.3%). Similar results were observed for the presence of hypertension (OR 1.97; 95%CI 1.48-2.45; p = 0.489, I<sup>2</sup> = 0.0%), increased glycated hemoglobin (OR 1.23; 95%CI 1.18-1.28; p = 0.924, I<sup>2</sup> = 0.0%), presence of diabetic nephropathy (OR 3.52; 95%CI 1.41-5.62; p = 0.335, I<sup>2</sup> = 0.0%), and increased age (OR 1.02; 95%CI 1.02-1.03; p = 0.479, I<sup>2</sup> = 16.6%) (Figure 4).

## DISCUSSION

This scoping review identified high heterogeneity among studies, leading to a wide variation in prevalence rates of DR, with differences between countries highlighted. The prevalence of this diabetic complication ranged from 21.0%<sup>(42)</sup> to 54.4%<sup>(9)</sup> for type 1 DM, both in Brazil. Type 2 DM varied from 18.8% in Mexico<sup>(27)</sup> to 47.1% in Brazil.<sup>(43)</sup> It may be related to the diagnostic method, age of the population studied, duration of disease, glycemic control, or other associated factors such as the presence of diabetic

**Table 5.** Risk factors for diabetic retinopathy

Risk Factor*	Longer DM duration	Presence of SAH	Increased Hb1Ac	Presence of DN	Increasing age
<b>Author</b>					
<b>Type 1 diabetes mellitus</b>					
Gomes MB, et al. <sup>(24)†</sup>	1.07 (1.05-1.09)	2.31 (1.65-3.25)	1.22 (1.19-1.35)		1.02 (1.01-1.03)
Melo LGN, et al. <sup>(31)†</sup>	1.07 (1.05-1.09)	1.68 (1.13-2.50)	1.24 (1.17-1.32)		1.03 (1.02-1.04)
Rodrigues TC, et al. <sup>(37)†</sup>	1.07 (1.03-1.11)	2.12 (1.16-3.87)		3.40 (1.89-6.13)	
<b>Type 2 diabetes mellitus</b>					
Cardoso CRL, et al. <sup>(19)†</sup>	1.29 (1.07-1.55)				
Cardoso CRL, et al. <sup>(12)†</sup>	1.04 (1.02-1.06)		1.30 (1.10-1.54)		
Santos KG, et al. <sup>(43)†</sup>	1.15 (1.09-1.22)		1.21 (1.01-1.46)	12.72 (3.89-41.56)	

\* (OR/RR; 95%CI); † original research articles, cohort or cross-sectional.

DM: diabetes mellitus; SAH: arterial hypertension; Hb1Ac: glycated hemoglobin; DN: diabetic nephropathy.



OR: odds ratio; 95%CI: 95% of confidence interval; DM: diabetes mellitus.

**Figure 4.** Meta-analysis factors associated with diabetic retinopathy by type of diabetes mellitus.

nephropathy or hypertension. Moreover, the different characteristics of health systems in the countries these studies took place, as well as the socioeconomic and cultural characteristics of health care specific to each region may have an important role when comparing the articles.

Regarding healthcare systems in Latin America, except for Brazil, Costa Rica, and Cuba, which adopt universal public system models, the other countries have segmented systems based on different insurance modalities.<sup>(49-51)</sup> In addition, eye diseases are not homogeneously distributed among Latin American countries due to the shortage of professionals, inequalities in coverage, fragmentation of services, and lack of integration in health systems.<sup>(3)</sup> Thus, these disparities may impact the early detection of DM and screening for DR, contributing to the differences in the prevalence of DR found in this study.

The decade of 1980 was marked by a major economic crisis that affected especially developing countries, including those in Latin America, which led to a reformulation of the actions of the State, mainly in the health sector.<sup>(52)</sup> These reforms deepened inequalities within and between countries that persist to this day and cause inequalities in access to health systems.<sup>(53)</sup>

The average prevalence of DR in Brazil was 32.7%, the highest among the countries studied. The country has a universal health system with a high degree of decentralization among the three levels of government, which may have led to a higher screening of this population.

Mexico presents a health system with segmented coverage of the population; the popular insurance receives insufficient federal funding and offers a restricted package of services, which excludes informal workers.<sup>(53)</sup> The country has a high prevalence of diabetes comorbidities and problems with the quality of care, which possibly contributed to the high average prevalence of DR (24.7%) observed in this review.

Peru has a fragmented system with a low degree of decentralization, in which the public sector predominantly serves the poor population who do not have health insurance, and EsSalud, which serves formal workers. Most eye care services are concentrated in the capital, where about 30% of the population lives. In 2014, the National Health Strategy and Blindness Prevention Plan: 2014-2019 was developed to reduce preventable blindness rates, including that due to DR, by improving the supply of eye health services, prevention, and rehabilitation actions, and strengthening epidemiological information systems.<sup>(54)</sup>

In Chile, the population coverage is universal for primary health care and segmented for curative care,

excluding informal workers and the self-employed. Since 1960, centers of eye care have been created within Primary Health Care to solve low-complexity diseases, leaving tertiary care for those of higher complexity. Recently, mobile units of eye care have also been implemented for users in remote regions, reducing the difficulties of access to the eye care network by the Chilean communities mostly in need.<sup>(55)</sup>

Colombia has universal coverage for primary care under implementation, with the creation of the Obligatory Health Plan. The low prevalence of DR found in the studies included in this scoping review may be underestimated, since this country does not have specific protocols for integral diabetes care, and little is known about the prevalence of diabetes and its complications, especially DR, among Colombians.<sup>(34)</sup>

Costa Rica has a decentralized universal health system, with health service provision organized in a pyramidal fashion according to levels of care and complexity.<sup>(49)</sup> The complications of diabetes, such as retinopathy, tend to be treated in tertiary-level hospital services due to the staggering of health care.<sup>(30)</sup> In 2002, the wait for care in ophthalmology outpatient clinics reached about 200 days, while the coverage of the diabetes care program served 47% of the target audience,<sup>(56)</sup> which possibly contributed to the low prevalence of DR in the country in this study.

In this review, it was not possible to identify studies in all Latin American countries, or indicators related to ocular health. The World Health Organization (WHO) developed the plan 'Universal eye health: a global action plan 2014-2019' to strengthen the collection of eye health indicators in partnership between political and health sectors, which highlighted another barrier to promoting more equitable eye health: the lack of national registries and standardized indicators for the roles of eye care professionals.<sup>(57)</sup>

The use of different diagnostic methods may also determine the prevalence found, because of the variation in sensitivity and specificity of each method. Slit lamp biomicroscopy and indirect ophthalmoscopy, under drug mydriasis, are the methods of choice for retinopathy research, because they show good results and are accessible to clinical practice. However, other tests can help in the diagnosis.<sup>(58)</sup>

Regarding the possible relationship between the type of diabetes and its influence on the prevalence of retinopathy, literature has already demonstrated an indirect relationship between these factors. The type of diabetes



directly interferes with the duration of the disease and the presence of diabetic nephropathy, regardless of the risk factors for the development of the complication.<sup>(59)</sup> Therefore, a higher prevalence of retinopathy is expected among type 1 diabetics, when comparing the same age group, given the higher precocity of diagnosis.<sup>(60)</sup>

Diabetic retinopathy is a microangiopathy characterized by increased vascular permeability, presence of exudates, hemorrhages, and capillary blockage in response to chronic exposure to high blood glucose levels and is classified into non-proliferative (RDNP) and proliferative, according to the absence or presence of abnormal vessels in response to areas of ischemia.<sup>(61)</sup> In this review, some papers presented a prevalence scaled by the severity of retinopathy. Esteves et al. observed that among patients with DR, 3.0% had severe non-proliferative form and 22.2% had the proliferative form, while Rodrigues et al. found the prevalences of 3.0% and 22.7%, respectively.<sup>(21,37)</sup> Martinez et al. saw that among the 15.0% overall prevalence, 5.8% had mild non-proliferative retinopathy; 3.9% had moderate NPDR; 4.7% had severe PNDR and 0.6% proliferative DR.<sup>(30)</sup>

Considering the risk factors observed for DR, the duration of diabetes has been consistently discussed, due to a longer time of exposure to hyperglycemia, which is the pathophysiological basis of the complication.<sup>(62)</sup> Similar to the results of this review, it has already been observed that each additional year of diabetes history increases the risk of developing DR by 8.0%.<sup>(63)</sup>

The presence of hypertension is also another known risk factor for the onset of DR. It is already established in the literature that hypertension, whether treated or poorly controlled/untreated, is associated with an increase in the onset of retinopathy in diabetic patients. This suggests that this patient can benefit from a more rigid control of blood pressure, seeking to prevent retinopathy.<sup>(64)</sup>

Another associated factor that was analyzed in one of the selected papers was masked nocturnal hypertension in patients with type 1 diabetes. The presence of masked nocturnal hypertension was associated with the occurrence of DR when adjusted for glycosylated hemoglobin, duration of diabetes, and the presence of nephropathy, increasing the risk by more than three times. These data reinforce the role of increased blood pressure as an important risk factor for DR, even in groups considered normotensive in routine assessments.<sup>(36)</sup>

In the present review, increased glycosylated hemoglobin was determined to be a risk factor for retinopathy for type 1 and type 2 DM. Rosa et al. observed that both

uncontrolled and variable glycosylated hemoglobin contributes to the increased risk studied. This finding reveals that not only adequate glycemia, but also stable glycemic control are important factors in preventing the microvascular complications of diabetes.<sup>(40)</sup>

Diabetic nephropathy was also seen as an important risk factor for retinopathy among both groups of diabetics, considering that the two diseases share an extremely similar pathophysiology, as microvascular complications of chronic hyperglycemia, such an association is expected.<sup>(65)</sup> In this regard, Saini et al. found similar results in their study, showing that the increase in severity of retinopathy and nephropathy increases proportionally in diabetic patients.<sup>(66)</sup>

The increase in age of the participants was also significant for the onset of DR, possibly due to the longer time of diagnosis and exposure to hyperglycemia.<sup>(37)</sup> Such association was also demonstrated in the prevalence analysis, since the extremes, higher and lower, were observed in the studies with higher and lower mean age, respectively.<sup>(42,9)</sup>

The influence of the socioeconomic level of the studied population was also evaluated as a risk factor by some authors, although not synthesized in a meta-analysis. As already reported by Alvares-Ramos et al. and Mendoza-Herrera et al., low socioeconomic and educational levels are important risk factors for DR, independent even of glycemic control.<sup>(67,32)</sup> In addition, literature has also shown that when patients have access to a private health-care service or the equivalent outside of Brazil, there is a considerable reduction in the rates of microvascular complications of diabetes, especially retinopathy.<sup>(32,24)</sup>

Esteves et al. also worked with risk factors related to the presence of a severe form of DR. They observed five main factors related to severe DR: hypertension, diabetic nephropathy, smoking, glycosylated hemoglobin level, and duration of diabetes (>17 years). The authors also noticed a syndemic effect, that increases prevalence with the accumulation of the exposure factors.<sup>(21)</sup>

This scoping review is a comprehensive evaluation of the evidence, incorporating all available published studies on the prevalence of DR and associated factors in Latin America. An important limitation encountered in conducting this review was the heterogeneity of the selected studies, making a more robust analysis of associated factors impossible. This can be justified by differences in study designs, forms of data collection and analysis, and differences in some characteristics of the populations, such as educational level and age. In addition, the lack of national eye health registries in the countries recognized

by the WHO itself makes it difficult to collect homogeneous data.

Many studies included people with both types of diabetes, making it difficult to assess the prevalence. Part of the studies was not retrieved (17 studies), because the full papers were not found in the searched databases and there was no response from the authors upon request. In addition, many ineligible papers were clinical studies, limited to a group not representative of the population. Finally, the absence of studies from several Latin American countries was also noted.

## CONCLUSION

The results of this scoping review reveal an important burden of diabetic retinopathy in Latin America and confirm the association of diabetic retinopathy occurrence with age, time living with the disease, metabolic control, and the presence of diabetic nephropathy and hypertension. In addition, it was noted that the prevalence of retinopathy may be further influenced by the population group that is studied and the diagnostic method used.

Disparities between health services in each country may also impact the early detection of patients with diabetes mellitus and screening for retinopathy, contributing to the differences found between prevalence rates. In addition, the lack of national registries and standardized indicators hinders the promotion of more equitable eye health.

Thus, it is necessary to reinforce the need for screening and interventions to prevent the onset/progression of diabetic retinopathy. We also emphasize the need for further studies in other countries, with standardization of indicators, enabling more homogeneous ocular care.

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## AUTHOR'S CONTRIBUTION

Joice Silva Machado: writing - original draft (equal); data analysis; writing - revision and editing (equal); Mariana Neves Brandão: writing - revision and edition (equal); Caroline Tianeze de Castro: writing - original draft (equal); data analysis; writing - revision and editing (equal); Trícia Silva Ferreira: writing - original draft (equal); writing - revision and editing (equal); Luiz Henrique Pitanga Evangelista dos Santos: Writing - original draft (equal); writing - proofreading and editing (equal); Danielle Souto

de Medeiros: Formal analysis (equal); supervision (leadership); writing - revision and editing (support).

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