



PREVALENCE OF HYPERTENSIVE RETINOPATHY AMONG YOUNG PEOPLE AND ADULTS IN DIRECT OPHTHALMOSCOPY

PREVALÊNCIA DA RETINOPATIA HIPERTENSIVA ENTRE JOVENS E ADULTOS NA OFTALMOSCOPIA DIRETA

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ABSTRACT: Objective: To identify the prevalence of hypertensive retinopathy among young people and adults diagnosed by direct ophthalmoscopy. Methods: This is an integrative review of bibliography in the databases Medline, Embase, Virtual Health Library and Cochrane Library, from a high sensitivity search strategy. Results: 593 articles were found, remaining 13 articles after the application of the inclusion criteria. Hypertensive retinopathy was present in more than 50% of the participants in eight articles. Regarding the epidemiological profile, four studies identified a higher incidence of hypertensive retinopathy in black people and males as risk factors for hypertensive retinopathy. Conclusion: The severity and time of diagnosis of systemic arterial hypertension showed a high correlation with the development of hypertensive retinopathy and the presence of hypertensive retinopathy may act in the stratification of cardiovascular risk regardless of levels pressure.

KEYWORDS: Diagnosis. Risk factors. Hypertension. Ophthalmoscopy. Hypertensive retinopathy.

RESUMO: Objective: To identify the prevalence of hypertensive retinopathy among young people and adults diagnosed by direct ophthalmoscopy. Methods: This is an integrative review of bibliography in the databases Medline, Embase, Virtual Health Library and Cochrane Library, from a high sensitivity search strategy. Results: 593 articles were found, remaining 13 articles after the application of the inclusion criteria. Hypertensive retinopathy was present in more than 50% of the participants in eight articles. Regarding the epidemiological profile, four studies identified a higher incidence of hypertensive retinopathy in black people and males as risk factors for hypertensive retinopathy. Conclusion: The severity and time of diagnosis of systemic arterial hypertension showed a high correlation with the development of hypertensive retinopathy and the presence of hypertensive retinopathy may act in the stratification of cardiovascular risk regardless of levels pressure.

PALAVRAS-CHAVE: Diagnosis. Risk factors. Hypertension. Ophthalmoscopy. Hypertensive retinopathy.

INTRODUCTION

Systemic arterial hypertension is a chronic non-communicable disease defined by systolic blood pressure greater than or equal to 140 mmHg and/or diastolic blood pressure greater than or equal to 90 mmHg. It has a multifactorial cause, associated with metabolic, structural and functional alterations¹.

A worldwide trend study of blood pressure, conducted between 1975 and 2015, concluded that the number of adults with systemic arterial hypertension in 2015 was 1.13 billion, highlighting higher prevalence in low-income countries due to population growth and aging². In Brazil, in 2018, the percentage of adults aged 18 to 59 diagnosed with systemic arterial hypertension was 32.3%. It was found that these numbers increased in the elderly population, reaching 71.7% in individuals over 70 years of age³. In the period from 2008 to 2017, 667.184 deaths attributable to systemic arterial hypertension were estimated as secondary causes⁴.

Its pathophysiology is associated with a genetic predisposition combined with several environmental factors, such as high sodium consumption, stress, sedentary lifestyle, alcoholism, among others. Nevertheless, the aging process also acts as a risk condition for the development of systemic arterial hypertension, due to the various physiological changes inherent in age progression, among them the stiffening of blood vessels⁵.

Once it is often asymptomatic, systemic hypertension is diagnosed late, which makes its treatment difficult and results in irreversible complications. The disease progression is related to functional and/or structural changes in target organs, such as brain, kidneys, heart and vessels. In this sense, it corresponds to the main modifiable risk factor for cardiovascular and renal disease⁶.

The mechanisms involved in the disease installation present endothelial dysfunction in common, characterized by imbalance between relaxation and constriction factors of the vasculature. In the face of this, the body tends to seek homeostasis, which generates a physiological disturbance that reflects on the chronic inflammatory state characteristic of the pathology⁷.

As a frequent target organ injury caused by the pathophysiology of systemic arterial hypertension, hypertensive retinopathy stands out, which is identified through the direct ophthalmoscopy technique and represents an important predictor of severity. The presence of this complication is confirmed by the detection of some changes during the fundus examination, namely: retinal hemorrhages, hard exudates, cotton spots and papilledema⁸.

Despite the scientific progress made in understanding systemic arterial hypertension and its complications, the pathogenesis of hypertensive retinopathy is not yet fully understood. The first findings of hypertensive retinopathy were described by Marcus Gunn in 1898, and since then other scholars have also identified predictors of retinal involvement. It is believed that the ophthalmological changes observed during systemic hypertension depend on four main factors: elasticity and resistance of the vessels, severity and duration of the disease⁹.

In 1939, the first classification of hypertensive retinopathy was developed by Keith, Wagener and Barker through a study conducted with untreated hypertensive patients. They compared the vascular histological alterations of a muscle tissue with the observed characteristics in the fundus, which allowed a division of retinal alterations into four stages: GROUP I - Arteriolar narrowing and alteration of the light arteriolar reflex; GROUP II - Arteriolar narrowing and alteration of the more pronounced arteriolar reflex and arteriovenous crossing; GROUP III - Alterations in group II, retinal and exudated hemorrhage; GROUP IV - Alterations in group III and papilledema¹⁰.

By this classification it was possible to associate the four groups with the severity of systemic arterial hypertension progressively, besides considering the patient's survival. Due to its numerous

benefits, it remains one of the most used scales to date. However, it is essential to carefully evaluate individual findings, since not all will follow this pattern concomitantly with the decompensation of the pressure levels¹¹.

The first manifestations in response to high blood pressure levels consist of vasoconstriction of retinal arterioles and increased vasomotor tone, which can be seen clinically as a generalized narrowing of the vessels. The persistence of this process leads to arteriosclerosis, which promotes thickening of the artery wall and decreased perfusion, evolving with vasospasms, pathological arteriovenous crossovers and retinal ischemia. If the retinal blood barrier is also reached, blood leakage to the retina may occur¹².

Besides having a high prognostic value because it is linked to the duration and severity of systemic arterial hypertension, hypertensive retinopathy also helps to differentiate a hypertensive urgency from a hypertensive emergency, since the presence of target organ injury discards the first. Nevertheless, several scores use hypertensive retinopathy to stratify a patient's cardiovascular risk, since the presence of retinopathy represents an alarm signal for the occurrence of stroke and hypertension nephropathia¹³.

Knowing the risks and correlation between hypertensive retinopathy and cardiovascular morbidity, scholars affirm that ophthalmoscopy should be performed annually in the monitoring of hypertensive patients to reduce the harmful effects of the disease. It is also an examination that can help in the diagnosis of systemic arterial hypertension when this is still unknown and accelerate the implementation of a suitable therapy to control the pressure values¹⁴. Thus, this evaluation methodology is understood as an important tool of subjective character, which can be used in spaces such as Primary Health Care aiming at the expansion of diagnostic capacity¹⁵⁻¹⁶.

Direct ophthalmoscopy is of low cost, quick to perform and allows several functions. In the outpatient routine, it allows the examiner to observe several morphological characteristics of the optic nerve, such as: color, shape, size and excavation. In addition, vascular arches, papilla, macula and retina can be evaluated. Given the vast potential of direct ophthalmoscopy, its use can help in identifying several visual alterations¹⁷.

That said, this research sought to identify the prevalence of hypertensive retinopathy among young people and adults diagnosed through direct ophthalmoscopy.

METHODOLOGY

This is a cross-sectional quantitative and descriptive research, developed through an integrative review of primary and retrospective bibliography. The elaboration of the research question was done through the PICO strategy, an acronym for P: population/patients; I: intervention; C: comparison/control; O: result/outcome. From the question, theme and objectives, a systematic literature review protocol was built for article searches.

Systemic arterial hypertension is considered a multifactorial disease of high prevalence worldwide that is associated with structural and/or functional changes in several organs. Among the target organ lesions resulting from its pathophysiological process is hypertensive retinopathy, characterized by lesions of the blood vessels of the retina that are identified by eye background examine⁷.

For the research, the databases used were: Pubmed, Embase, Cochrane and Virtual Health Library – BVS in Portuguese.

The search in the databases was performed from December 2021 to March 2023. The official descriptors Ophthalmoscopy, "Ophthalmoscopy", Hypertension and "Hypertension" were used, as well as their synonyms. For the Pubmed and Cochrane databases, descriptors from the "Medical Subject Headings" (MeSH) were used. For the research at BVS, the platform of "Health Science Descriptors" (DeCS) was used. And for the Embase were searched in "Elsevier's authoritative life science thesaurus" (Emtree).

During the search, the Boolean operators "OR" and "AND" were used. No filters were applied during the research, so there was no time restriction of the works.

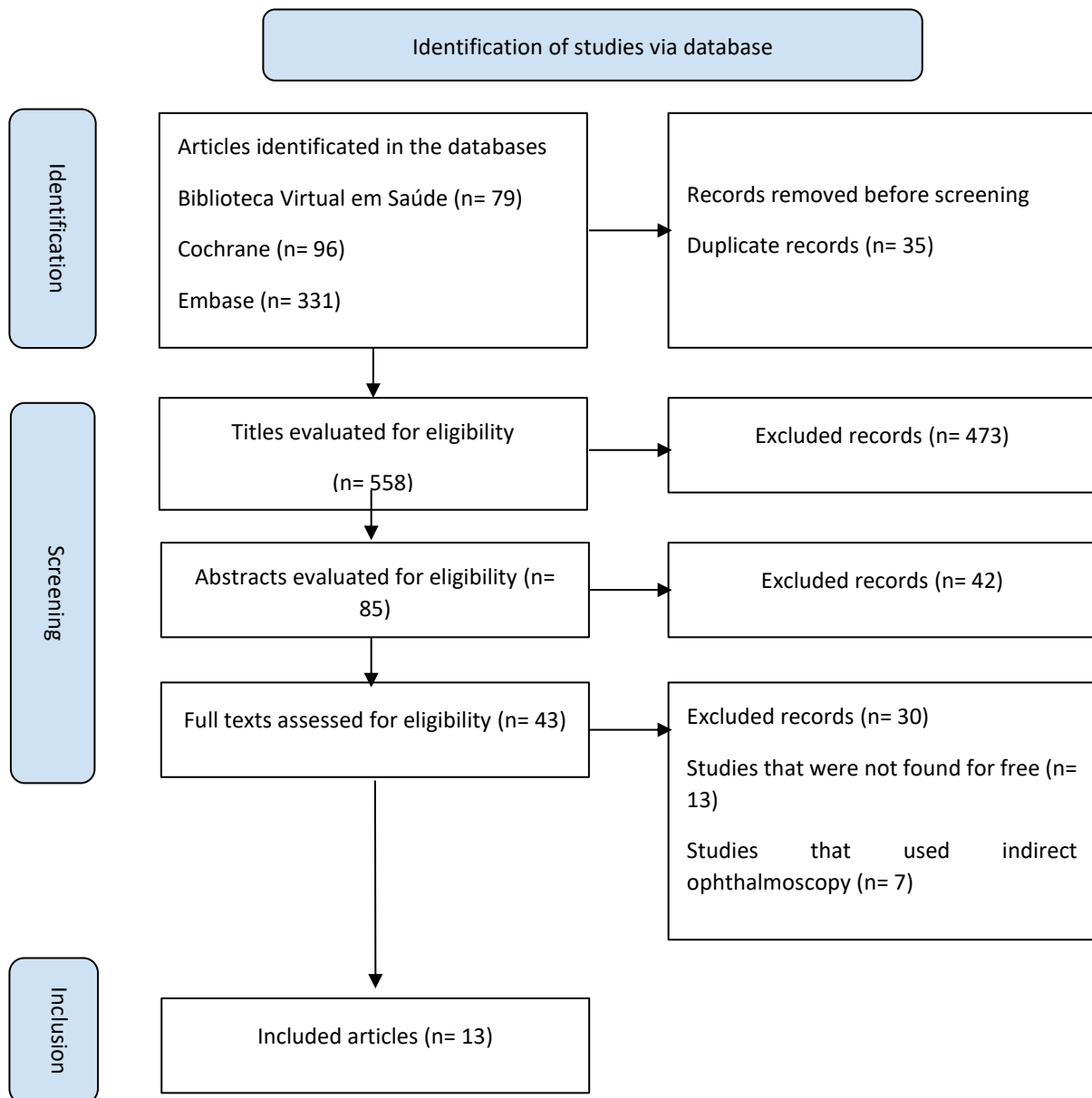
The inclusion criteria were: use primary data and involve human beings. The exclusion criteria were: use indirect ophthalmoscopy as a diagnostic method and not present a relation with the subject of interest. The target audience of the research involved humans between 18 and 59 years old who were submitted to the direct ophthalmoscopy examination. The age restriction was justified by gaps in research on this topic that addressed the younger audience. In addition, some studies have concluded that the relationship between hypertensive retinopathy, systemic arterial hypertension and cardiovascular risk is stronger in people younger than 60 years old¹⁸⁻¹⁹.

After the application of the search strategy in the four databases, 593 articles were found, which were extracted and inserted into the RAYYAN intelligent review platform. Within the platform, 35 duplicates were deleted and the remaining 558 records had their titles read individually.

Through a thorough analysis of the 558 titles, 473 papers were eliminated in the first stage of screening for not presenting a relationship with the proposed theme. Then, 85 papers were read in full, of which 42 were excluded because they did not meet the inclusion and/or exclusion criteria determined previously, leaving 43 papers for complete reading.

During the complete reading of the 43 selected records, 13 works were not found on any free platform, which reflected in their exclusion. In addition, 17 more articles were removed, of which seven used indirect ophthalmoscopy as a diagnostic method for hypertensive retinopathy and eight had insufficient data.

In this sense, 13 articles were considered eligible for the implementation of this integrative review. Figure 1 shows a flowchart that summarizes the steps of article selection, which was based on the recommendations of the PRISMA protocol²⁰.

Figure 1 - Flowchart of the route to obtain selected studies according to the PRISMA recommendation, Mossoró/RN, 2022.

The analysis of the 13 articles included was guided by a standardized data collection instrument²¹. The collected data were separated and organized in a spreadsheet built in the Excel program, version 2019. Then, a comparison of the parameters used in the registration of the studies was carried out, such as the prevalence of hypertensive retinopathy diagnosed by direct ophthalmoscopy, the epidemiological profile of the patients studied, the methodological criteria of the limits and/or identified ways with potential to interfere in the reliability of results, among others.

RESULTS

The identification of the 13 articles included in the research is expressed in Table 1, which shows the general characteristics of the papers, such as journal, year of publication, country, language and type of study. As for the language of the papers, four were published in Portuguese, two in Spanish and seven in English. Regarding the type of study, according to the classification established by the respective

authors, six cross-sectional studies, four prospective studies, two cohort studies and a retrospective study were identified (Table 1).

Table 1 - Identification of the 13 articles included in the research, Mossoró/RN, 2022.

Periodical	Year	Country	Idiom	Type
Revista Cubana de Medicina	1977	Cuba	Spanish	Cross-sectional
Arquivos Brasileiros de Oftalmologia	1994	Brazil	Portuguese	Cross-sectional
Arquivos Brasileiros de Oftalmologia	1997	Brazil	Portuguese	Prospective
Revista Cubana de Medicina	2000	Cubau	Spanish	Cross-sectional
Arquivos Brasileiros de Oftalmologia	2002	Brazil	Portuguese	Prospective
The British journal of ophthalmology	2002	Singapore	English	Cohort
Kathmandu University medical journal	2003	Nepal	English	Prospective
Saudi Medical Journal	2006	Iran	English	Cross-sectional
Journal of vascular and interventional neurology	2008	United States	English	Cohort
Arquivos Brasileiros de Cardiologia	2010	Brazil	Portuguese	Cross-sectional
Journal of human hypertension	2010	Netherlands	English	Retrospective
Clinical and experimental hypertension	2011	Kosovo	English	Prospective
Clinical and experimental hypertension	2020	United States	English	Cross-sectional

Table 2 shows the number of participants studied by the studies, as well as their epidemiological characteristics, such as gender, age and race. From a simple numerical sum, it was concluded that the total of hypertensive patients submitted to direct ophthalmoscopy examination in all articles was 8,334.

Table 2 - Epidemiological aspects of study participants, Mossoró/RN, 2022.

Article	No. of participants	Gender		Age
		Male	Female	
1	99	Not described	Not described	Not described
2	1,741	38.60%	61.40%	40-60 years
3	51	Not described	Not described	< 50 years
4	111	42.30%	57.70%	MA: 52 years
5	119	21.80%	78.20%	MA: 51 years
6	92	33.70%	66.30%	Not described
7	213	44.60%	55.40%	MA: 45 years
8	302	43.78%	56.22%	30-60 years
9	560	100%	0%	35-59 years
10	200	57.00%	43.00%	31-40 years
11	56	32.14 %	67.86 %	MA: 55 years
12	4,753	39.34%	60.66%	MA: 56 years
13	28	32.14%	67.86%	MA: 50 years

Due to the restriction of age group defined previously, the selected studies were those that involved people aged 18 to 59 years. Corroborating with this, Toledo and collaborators²⁰ also delimited their research sample to under 50 years of age, in order to evaluate the changes caused by hypertensive retinopathy without interference of ophthalmological manifestations caused by senility and atherosclerosis.

The percentage of male and female audiences diverged in all studies, it was not possible to conclude a general statistic because some authors did not specify the sex of patients (articles 1 and 3), while others opted to cover only one gender (article 9). Furthermore, it should be emphasized that few studies attributed a greater prevalence of hypertensive retinopathy in certain sex.

Regarding the race of patients, four out of 13 studies identified a higher incidence of hypertensive retinopathy in the black race and none identified a higher incidence in the white race.

All articles analyzed opted for the classification of Keith, Wagener and Barker¹⁰. Table 3 presents the prevalence data of hypertensive retinopathy and the time of diagnosis of systemic arterial hypertension according to what was stated by the authors.

Table 3 - Prevalence of hypertensive retinopathy and time of diagnosis of systemic arterial hypertension in selected articles, Mossoró/RN, 2022.

Article	Prevalence of hypertensive retinopathy	Time of diagnosis of systemic arterial hypertension	
		< 10 years	>10 years
1	>90.00%	63.60%	36.40%
2	23.00%	35.83%	64.17%
3	>90.00%	58.0%	42.00%
4	82.00%	100%	0.00%
5	84.00%	72.30%	27.70%
6	11.60%	49.90%	51.10%
7	39.90%	0.00%	100%
8	63.57%	84.75%	15.25%
9	11.60%	Not described	Not described
10	74.50%	36.70%	64.30%
11	94.60%	14.30%	85.70%
12	24.49%	71.06%	38.94%
13	68.00%	59.00%	41.00%

The variation among the prevalence found can be justified by the selection of subjects, given that the studies with lower indices (articles 2, 6, 9 and 12) used control groups or a larger sample and did not differentiate the findings between normotensive and hypertensive participants, which may hinder the analysis of the exposed data.

A total of ten out of 13 articles analyzed linked a high percentage of hypertensive retinopathy to patients who diagnosed systemic arterial hypertension for longer. Toledo et al.²² identified a higher

frequency of pathological arteriovenous crossovers and tortuosity of the vessels in participants who treated systemic arterial hypertension for more than ten years. Bakalli et al.²³ showed that generalized retinal arteriolar narrowing and arteriovenous crossover are signs of long-standing systemic arterial hypertension.

All studies found a higher prevalence of mild retinopathy. In the 13 analyzed, patients diagnosed with hypertensive retinopathy grade IV represented less than 20%. Figueiredo Neto et al.²⁴ emphasized that the low frequency of severe retinal signs is due to regular treatment and blood pressure control of systemic arterial hypertension, which are currently better adhered to by society.

Considering the negative effects of systemic arterial hypertension on its main organs-target, Duncan et al.²⁵ demonstrated that the presence of hypertensive retinopathy represented a twice as high risk of death from cardiovascular disease or myocardial infarction regardless of blood pressure levels. Furthermore, Suri and Qureshi²⁶ observed that the vascular examination of the retina may act as a predictor of cardiovascular events and should be included in the routine evaluation of these patients.

The remaining articles also correlated retinal findings with aortic atherosclerosis, left ventricular hypertrophy, hypertensive encephalopathy, kidney disease and encephalico^{23,27}.

An important limitation of some studies analyzed was the diagnosis of dyslipidemia in patients studied through laboratory tests performed during the execution of the work, since such comorbidity contributes to the development and progression of retinal dysfunction in many eye diseases²⁸. Thus, certain results presented here may have been masked and/or overestimated, since the authors did not restrict the participation of these patients.

Regarding the execution of the examination, only five articles clarified that the examiners did not know the clinical condition of the patients in question. When the examiner knows that he is facing a hypertensive person, he tends to overestimate the findings of arteriolar narrowing in the eye of the examined patient, which may act as a bias during the classification of retinopathy degrees. In contrast, direct ophthalmoscopy was recognized as an adjuvant factor in determining the anti-hypertension therapeutic aggressivity²⁹.

The study by Duncan et al.²⁵ enforced the use of direct ophthalmoscopy for risk stratification in determining the prognosis of systemic arterial hypertension, even in patients with blood pressure levels compatible with the milder stages of the disease. Similarly, Karki³⁰ was characterized as the best tool for the diagnosis of retinal alterations, corroborating with Yildirim et al.³¹ who supported the use of the instrument in the care of patients with masked hypertension.

The study by Sakata et al.³² concluded that retinal findings can serve as a warning to the physician regarding the stage of systemic arterial hypertension in which the patient is since the presence of hypertensive retinopathy is an excellent indicator of target organ injury. Although the effectiveness of other laboratory tests is known in this screening, direct ophthalmoscopy has low cost, easy execution and can be performed at the first visit.

DISCUSSION

One finding relevant to the year of publication of the papers was that, of the 13 selected, only one was published in the last decade, the rest are from previous years, which shows the lack of current studies on hypertensive retinopathy diagnosed by direct ophthalmoscopy.

The scientific progress, the transformation of the population age pyramid and the acquisition of new means of information are factors that have repercussions on the clinical course of diseases each

year. Thus, the analysis of work carried out in previous decades may be biased, since there were significant advances in the diagnosis and treatment of systemic arterial hypertension. These changes directly reflect on the prevalence and predictive significance of retinal findings.

Regarding the restriction of age group of participants, it is conceptualized that younger patients are more likely to develop more severe stages of retinopathy. This can be explained by the absence of chronic compensatory mechanisms that are acquired in later ages. Thus, elderly patients may be underrepresented in the studies due to increased mortality inherent in the age³³.

A higher predominance of females over males is observed when the studies are reviewed in general, and may be associated with a higher prevalence of uncontrolled hypertension among women²³. Contributing to this, another study concluded that although blood pressure levels are lower in men, hypertensive retinopathy prevails in males (69.8%) when compared to females (30.2%)³⁰.

Considering that systemic arterial hypertension is multifactorial and directly linked to the cardiovascular system, the influence of sex on the clinical prognosis of patients also perpetuates in heart disease. A cohort study of 560 hypertensive men found that the presence of hypertensive retinopathy was associated with a twice as high risk of coronary heart disease in the male population²⁵.

Regarding race, Toledo et al.²² found that 68.3% of individuals with retinal findings consistent with hypertensive retinopathy belonged to the black race, while Molina³⁴ found a greater presence of degrees III and IV of hypertensive retinopathy in black individuals. These results can be justified, in large part, by the prognosis of systemic arterial hypertension, which tends to be more severe in this population³⁵.

Concerning the prevalence of retinopathy, eight studies found the presence of hypertensive retinopathy in more than 50% of patients, pointing to a high prevalence of this finding in the context of systemic arterial hypertension. This result is compatible with a review study that highlighted the influence of hypertensive pathophysiology in the development of several threatening vision problems, including which reaffirms the need for close partnership between ophthalmologists and general practitioners in terms of prevention of these diseases³⁶.

The severity of hypertension was also significant in the analysis of the prevalence of retinal findings, since nine of the 13 articles associated higher blood pressure values – corresponding to stages 2 and 3 of systemic arterial hypertension – with more advanced degrees of hypertensive retinopathy, the authors attributed this to the fact that these patients are more exposed to inflammatory complications of hypertension, which results in the precursor endothelial dysfunction of retinopathy²⁹.

In accordance with this, a survey conducted with 200 hypertensive patients hospitalized identified the presence of hypertensive retinopathy in 74.5% of them. The findings compatible with grade IV retinopathy were found in 2.5% of this public, all of which presented electrocardiographic alterations suggestive of left ventricular hypertrophy and presence of pathological q waves. In addition to laboratory tests indicating chronic kidney disease caused by decompensated systemic arterial hypertension³⁴.

Current statistics on chronic kidney disease indicated that the degree of hypertensive retinopathy increases as glomerular filtration rate decreases. A survey of non-diabetic renal patients concluded that 96.8% of patients with stage 4 retinopathy were classified as stage 5 chronic kidney disease, suggesting that severe retinopathy is strongly associated with renal complications³⁷.

Another study showed that among patients with mild hypertension, 25.3% had direct ophthalmoscopy findings indicative of hypertensive retinopathy. In patients with moderate stage, this percentage was 34.5%. In those who did not perform the recommended treatment of the disease and

were classified as a severe stage of systemic arterial hypertension, the prevalence of hypertensive retinopathy was 84.6%³⁸.

Similarly, a more recent study found an intimate link between retinal arteriolar narrowing and increased blood pressure, in which each 10 mmHg increase in systolic blood pressure was associated with a 0.9 μ m narrowing of the arteriolar³⁹.

About the direct ophthalmoscopy, it was found that even being faced with numerous technological advances and new techniques in development, which require a shorter time of light incidence in the patient's eye, as well as greater freedom for the examiner, The researchers still recognize that the advantages of the exam exceed its limitations, which justifies its defense in the current context⁴⁰.

CONCLUSION

It was concluded that most medical students do not have the mastery to exercise the technique properly due to underutilization of the ophthalmoscope during medical training. Therefore, the improvement of direct ophthalmoscopy teaching is of great importance in the qualification of professionals, to broaden the perspectives of differential diagnoses through an ophthalmological evaluation and offer patients the opportunity for early detection and treatment of limiting conditions, especially systemic arterial hypertension, contributing to the promotion of population health and improvement of quality of life in the long term⁴².

Most studies found a high prevalence of hypertensive retinopathy in patients with hypertension. A higher frequency of retinal alterations was directly correlated with the time of diagnosis and severity of systemic arterial hypertension. It is also observed that the presence of hypertensive retinopathy may act in the stratification of cardiovascular risk regardless of blood pressure levels. It is also concluded that the male gender and black race may represent risk factors for the development of hypertensive retinopathy. All these findings reinforce the importance of this technique to increase the ability to identify changes, and can be applied in the practice of outpatient services and Primary Health Care.

Despite the numerous technological advances and new techniques being developed, direct ophthalmoscopy is still an important tool in the diagnosis of hypertensive retinopathy. Its execution was recognized as an adjuvant factor in the determination of anti-hypertensive therapeutic aggressiveness of hypertensive retinopathy. It is thus an important technique aimed at improving health promotion among people with increased risk for the development of retinopathy, if used in a proper and routine way by health services.

Among the results found, there is a clear lack of updated studies on the subject, which indicates a need for new research to reassess the prevalence of hypertensive retinopathy, as well as its predictive value against the diagnosis of systemic arterial hypertension. It is important to note that the next studies involving direct ophthalmoscopy examination ensure that the examiner does not know the clinical picture of the patient in question, to avoid overestimation of ophthalmological findings.

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