Abstract

Background: Our objective was to estimate the frequency of anisometropia at various educational stages, from pre-school to 9th school year, studying its association with gender, study cycle and area of residence.

Methods: 749 children and adolescents (from 3 to 16 years old) participated in this study, 46.7% girls and 42.7% living in a rural environment. The refraction was performed with a paediatric, open field autorefractometer (PlusOptix), without cycloplegic and under binocular conditions.

Results: The frequency rate of anisometropia in the studied sample was 6.1%, varying from 2.9% in pre-school education to 9.4% in the 3rd study cycle. Myopic anisometropia was the most frequent and hyperopic and astigmatic anisometropia showed identical proportions of occurrence. No statistical evidence was found to state that the occurrence of anisometropia differs between genders or between areas of residence. Regarding the school cycle, a significant association was found with spherical equivalent anisometropia, with an increase in its frequency with school progress (p=0.012), with myopic anisometropia being the main contributor to this variation.

Conclusions: The increase in workload for near tasks has been identified as a risk factor for the increase in myopia. This fact may be related to the increase in anisometropia with the educational stage, found in this study. The high rate of anisometropia found in adolescents (9.4%) as well as the progressive increase in this rate throughout school progress (from 2.9% to 9.4%) suggests the need to extend the detection strategies of this condition to beyond childhood.

Keywords
Pediatrics, Child, Teenager, Refraction, School vision
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Author roles: Nunes AF: Conceptualization, Data Curation, Formal Analysis, Investigation, Methodology, Project Administration, Resources, Software, Supervision, Validation, Visualization, Writing – Original Draft Preparation, Writing – Review & Editing; Batista M: Data Curation, Formal Analysis, Investigation, Resources, Writing – Original Draft Preparation; Monteiro P: Conceptualization, Methodology, Project Administration, Supervision, Validation, Visualization, Writing – Review & Editing

Competing interests: No competing interests were disclosed.

Grant information: The author(s) declared that no grants were involved in supporting this work.

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Introduction

Anisometropia is an ocular disorder characterized by an interocular difference (IOD) in refractive error, representing a specific refractive condition insofar as the two eyes of an individual, with presumably similar sociodemographic, environmental and genetic influences, can have asymmetric eye growth.\(^1\) This condition can occur in situations of myopic, hyperopic or astigmatic asymmetry and is strongly associated with the development of other eye changes such as aniseikonia, amblyopia, diplopia and strabismus.\(^2,3\)

Although there is no uniformly defined dioptre value for its clinical classification, an IOD in the spherical equivalent (SE) of 1 diopter or more is accepted as the threshold, for most authors.\(^1,4-8\) However, even using this limit, the scientific literature presents a significant variation in the prevalence values of anisometropia in terms of age, gender and ethnicity.\(^4,5,8,9\) Factors associated with lifestyle and educational level have also been referred to as risk factors for anisometropia.\(^7,8,10\)

Early detection and early treatment is crucial to prevent permanent visual loss. Although it is not clear what is the ideal age to perform the correction, in order to guarantee an ideal visual development and maturation,\(^11\) the early correction of anisometropia is important, either because it prevents the development of other changes such as aniseikonia, amblyopia and strabismus,\(^3,12,13\) and even in small degrees (<1D) facilitates emmetropization,\(^11\) whether because it improves quality of life, reducing or eliminating symptoms of visual discomfort. In this way, visual screening at a young age is useful in identifying who is most likely to benefit from early optical correction or preventive treatment.\(^11,14,15\)

The clinical methods used to characterize anisometropia are refractive techniques, with autorefraction, using Plusoptix, one of the most recommended techniques for screening activities.\(^16,17\) This instrument allows quantifying the refractive error in open field, simultaneously in both eyes and under the same conditions, in a fast, easy, safe, non-invasive way, in which it is possible to obtain a very similar value to that obtained by cycloplegic refraction\(^17-19\) and with excellent precision in anisometropia signalling.\(^19\)

Scientific studies on the prevalence of anisometropia focus on children or adults, with less research being found in adolescence. There is evidence that lifestyle, as well as educational level, may be risk factors for its development. The aim is to estimate the frequency of anisometropia (spherical and astigmatic) and to analyse its pattern of variation in a sample of children and adolescents, from preschool education (from three to six years old) to the various cycles of basic education (from the 1st to the 9th school year in Portugal, from six to fifteen years old).

Methods

749 children and adolescents aged between three and sixteen years participated. Students' data for which it was not possible to obtain refraction were excluded, due to technical issues associated with the performance of the instrument (presence of strabismus, opacities, retinal anomalies or when the refractive error exceeded the instrument's measurement limit - spherical measurement range or cylindrical from \(-7.00\) to \(+5.00\)D) or due to lack of cooperation from the participant.

The refractive error was obtained with the paediatric autorefractometer model A09 by PlusOptix by the average of three consecutive measurements, binocular and without the use of a cycloplegic. The PlusOptix allows measuring the refractive error in real time and in both eyes at the same time, at a distance of one meter from the subject's eyes.

Data analysis

In order to calculate the average of the three refractive measurements, the power was converted from its spherical-cylindrical to its vector representation, described by Thibos,\(^20\) using the following expressions:

\[ SE = S + \frac{C}{2} \quad (1) \]

\[ J_0 = \left( -\frac{C}{2} \right) \cos (2\alpha) \quad (2) \]

\[ J_{45} = \left( \frac{C}{2} \right) \sin (2\alpha) \quad (3) \]

Where SE represents the spherical equivalent; \(J_0\) represents Jackson's crossed cylinders on the 90° or 180° axis, \(J_{45}\) represents Jackson's crossed cylinders on the 45° or 135° axis, \(S, C\) and \(\alpha\) represent the spherical, cylindrical and cylinder axis component, respectively, of the autorefractometer measurement.
Refractive state classification
The participants were classified in emmetropes, myopes, hyperopes, astigmats or anisometropes, according to the average value of the autorefractometer. In order to carry out this classification, the criteria recommended for the autorefractometer used were applied (Table 1).

Anisometropia classification
The absolute value of IOD of the refractive error in terms of SE was designated as spherical anisometropia (SA), the absolute IOD in astigmatism was designated as meridional anisometropia (MA) and the absolute IOD only in the astigmatic component was designated by simple meridional anisometropia (sMA), according to the cutoff points referred to in Table 1. The presence of at least one of the previous conditions was designated as total anisometropia (TA). Low anisometropia was considered for IOD values below 2.00D, high anisometropia for values between 2.00D and 6.00D and very high anisometropia for IOD values above 6.00D.

According to the type of refractive error, anisometropia was classified as myopic, when both eyes were myopic or when one eye was myopic and the other was emmetropic; hyperopic, when both eyes were hyperopic or when one eye was hyperopic and the other emmetropic; antimetropic, when one eye was myopic and the other hyperopic; simple meridional anisometropia when there was no SA, but there was MA.

Statistical analysis
A descriptive statistical analysis was carried out, using SPSS version 26 package, characterizing the sample in the variables of interest, sociodemographic and refractive, presenting means and standard deviations, frequencies and percentages both in the whole of the sample and also according to several stratifications to which it was subjected.

In all the sociodemographic factors in which the sample was categorized, groups with a large size (n > 30) were obtained and by applying the central limit theorem, it can be considered that the violation of the assumptions does not have serious consequences. Thus, the age differences between the groups were inferred by parametric tests: student’s t when the factor subdivides the sample into two groups and one way ANOVA when the factor subdivides the sample into more than two groups. To test the independence between two qualitative variables, the Chi-square independence test was applied.

All the results of the statistical inference tests were interpreted to a 95% confidence level, that is, the significance level of 0.05 was used.

Ethics approval
This study was conducted in accordance with that the principles of the Declaration of HELSINKI and written informed consent were obtained from parents of each participant in the study. It was approved by the Ethics Committee from Universidade da Beira Interior (CE-UBI-Pj-2019-043).

Consent to participate
Written informed consent was obtained from parents or legal guardians of all participants.

Results
Sample characterization
In Portugal the compulsory education includes basic education, which is divided into 3 cycles, followed by the secondary education. The 1st cycle of basic education includes the 1st to 4th school year (ages 6 to 10), the 2nd cycle includes the 5th and 6th year (ages 10 to 12) and the 3rd cycle includes the 7th to the 9th year (ages 12 to 15). The sample under study had students from preschool to the 3rd cycle of basic education and was characterized according to gender, area of residence and cycle of studies. Table 2 summarizes the characteristics of the sample.

<table>
<thead>
<tr>
<th>Refractive state</th>
<th>&lt; 6 years old</th>
<th>≥6 years old</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emmetropes</td>
<td>−1.00D &lt; SE &lt; +1.25D</td>
<td>−1.00D &lt; SE &lt; +1.00D</td>
</tr>
<tr>
<td>Myope</td>
<td>SE ≤ −1.00D</td>
<td></td>
</tr>
<tr>
<td>Hyperope</td>
<td>SE ≥ +1.25D</td>
<td>SE ≥ +1.00D</td>
</tr>
<tr>
<td>Astigmat</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anisometrope</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| Classification criteria for refractive state [17] 16. |

<table>
<thead>
<tr>
<th>Refractive state</th>
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<tr>
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<td>SE ≥ +1.25D</td>
<td>SE ≥ +1.00D</td>
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<td>Astigmat</td>
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<td></td>
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<tr>
<td>Anisometrope</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| Table 1. Classification criteria for refractive state [17] 16. |
It can be seen that the sample has a similar average age between genders and between area of residence, but as can be expected, ages differ between study cycles, being higher in more advanced cycles, and this difference is statistically significant.

Refractive state

According to the classification criteria previously defined for the classification of refractive state, it was concluded that in the study sample 71.16% (n = 533) is emmetropic. Among subjects with significant refractive error (n = 216), it was found that hyperopia is the most frequent refractive error (50.5%, corresponding to 14.6% in the studied population) followed by myopia (22.7%, corresponding to 6.5% in the population), anisometropia (21.3%, corresponding to 6.1% in the population) and astigmatism (11.6% (n = 25) where 5.6% are cases of simple astigmatism and 6% compound astigmatism, corresponding to 3.3% in the population). Figure 1 shows graphically the distribution of the different refractive states in the study sample. The representation of astigmatism, refers only to the occurrence of simple astigmatism, without a significant SE.

Anisometropia

46 participants with anisometropia were identified (6.1% of the studied population). According to the magnitude of the refractive error, no child was found with very high anisometropia, 15 were registered with high anisometropia and 31 with low anisometropia, that is, of the anisometrope subjects, most (67.4%) had low anisometropia.

In the classification of anisometropia according to the type of refractive error, 37 subjects (80.4% of anisometropes, corresponding to 4.9% in the studied population) were found with SA, integrating 21 with myopia, 15 with hyperopia and 1 with antimetropia; and 15 subjects (32.6% of the anisometrope sample, corresponding to 2% in the population) with MA, and only 9 of these did not have SA, and it can be considered that about 20% of the anisometrope sample presents simple meridional anisometropia (sMA). This distribution is represented graphically in Figure 1. It is possible to observe that myopic anisometropia is the most frequent (46%), followed by hyperopic anisometropia (33%) and sMA (19%). Antimetropic anisometropia is the least frequent (2%).

Influence of sociodemographic variables

The proportion of subjects with anisometropia was analysed according to gender, area of residence and school cycle, and through the Chi-square test it was evaluated whether these variables are associated with the occurrence of anisometropia in the studied population (Table 3). The Chi-square test indicates that there is no association between sMA and any of the factors under analysis, therefore this parameter is not in the table.

No significantly different occurrence of anisometropia was found according to gender or area of residence. (p > 0.05), however, in relation to the school, there is a pattern of variation that increases with the cycle of studies, ranging from 2.9% in preschool education to 9.4% in the 3rd cycle of studies, however this association is only statistically significant for SA ($\chi^2(3) = 10.918; p = 0.012$), where there is a rate of 1% in preschool education and 8.6% in the 3rd cycle. It should be noted that the study cycle is dependent on age, as shown in Table 2, older children attend the more advanced study cycle.

<table>
<thead>
<tr>
<th>Factor</th>
<th>Sample dimension N (%)</th>
<th>Age</th>
<th>Statistical test</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Average ± SD</td>
<td></td>
</tr>
<tr>
<td>Total sample</td>
<td>749 (100%)</td>
<td>9.6 ± 3.3</td>
<td>---</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>399 (53.3%)</td>
<td>9.7 ± 3.2</td>
<td>t(747) = 0.903; p = 0.367</td>
</tr>
<tr>
<td>Female</td>
<td>350 (46.7%)</td>
<td>9.5 ± 3.5</td>
<td></td>
</tr>
<tr>
<td>Residence area</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rural</td>
<td>320 (42.7%)</td>
<td>9.8 ± 3.3</td>
<td>t(741) = 1.662; p = 0.097</td>
</tr>
<tr>
<td>Urban</td>
<td>423 (56.5%)</td>
<td>9.4 ± 3.3</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>6 (0.8%)</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Study stage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preschool</td>
<td>103 (13.8%)</td>
<td>4 ± 0.9</td>
<td>F(3;745) = 2177.4; p &lt; 0.001**</td>
</tr>
<tr>
<td>1st cycle</td>
<td>231 (30.8%)</td>
<td>7.6 ± 1.2</td>
<td></td>
</tr>
<tr>
<td>2nd cycle</td>
<td>181 (24.2%)</td>
<td>10.6 ± 0.9</td>
<td></td>
</tr>
<tr>
<td>3rd cycle</td>
<td>234 (31.2%)</td>
<td>13.2 ± 1.1</td>
<td></td>
</tr>
</tbody>
</table>

**Significant at the 0.01 level.
Figure 2 illustrates the distribution of anisometropia according to the type of refractive error, for each school cycle. It is observed that myopic anisometropia is present in all study cycles, registering a considerable increase from the beginning of school, that is, from the 1st cycle to the 3rd cycle. On the other hand, hyperopic anisometropia was manifested on a larger scale in children of the 1st cycle, with a lower occurrence in the following cycles. As for the simple MA, it is present in all study cycles and there is no specific pattern in its variation with the study cycle progress.

Discussion
The present study was carried out with students, including students from preschool education (three years old) to the 9th school year (~fifteen years old) and the value of the IOD considered was \( \geq 1.25 \text{D} \), as it is the suggested value for the interpretation of the results obtained with the material used. An anisometropia rate of 6.1% was found, considering the spherical and meridional anisometropia. It was found that this rate varies with the cycle of studies, showing an increase as the level of education advances, ranging from 2.9% in preschool education to 9.4% in the 3rd cycle of basic education and...
no statistically significant differences were found in the distribution of anisometropia either between genders or between areas of residence. It was also found that myopic anisometropia was the most prevalent (46%), with a considerable increase in the 3rd cycle of studies.

Comparing with others studies, some authors point to a frequency similar to the one found on this research,4,7,8,11,21 others point to a lower frequency22 and others still refer to a higher frequency.23,24 Studies that included only children aged five and six years report rates of 1.3% and 1.6% (SA).5,22 The frequency of SA, found in the present study, in preschool education (children from three to six years old) was 1%, this value being closer to those studies. Others studies included participants from 15 to 19 years old and report rates of 11.2% for SA.23 For the 3rd cycle of studies (average between 12 and 15 years of age), the present study indicates a frequency of 8.6% (SA) and according to the observed variation pattern, at a more advanced age and school stage, a higher rate is expected.

Geographical and methodological issues make it difficult to compare prevalence studies. There is a pattern of greater variability in studies on the Asian continent, where for an identical age group, there are records ranging from 2.5%22 to more than 10%;7 however this is the continent where more studies on the subject are found. In Europe, more similar results are found, 4,6% and 6,9%.4,11

In the literature, the pattern of variation of anisometropia as a function of age and during the school period is not clear, presenting discordant results. Although many studies focus on children, it is common to have relatively wide age ranges. Most authors conclude that anisometropia varies with age,5,7,26 although there are also studies where this relationship has not been found.10,13 Studies on the subject, at school age, which showed an increasing prevalence with age were carried out in populations with a high frequency of myopia, a condition whose prevalence increases in adolescence.26 On the other hand, longitudinal studies show that the prevalence of anisometropia increases after children start attending school.5,7,21 Given these two lines that justify the variation of anisometropia during school age, it appears that they are related to each other, since the progress in the school path is accompanied by increasing age. In the present study, an anisometropia frequency was also found to increase with advancement in the level of education, and consequently the age factor is also contributing to this situation, with myopic anisometropia being the one that most contributes to this variation pattern.

Regarding the influence of gender on anisometropia, contradictory data are found in the scientific literature, while in one study it is reported that the prevalence found was higher in males26 in others it is reported that the prevalence rates are higher in females.10,24 The results of the present study reveal a higher frequency in females (7.1%) than in males (5.3%), however these differences are not statistically significant, and this finding is in line with the results of other authors.9,13,21,25

The influence of living in rural or urban areas has also been the object of study by several researchers, considering the development of myopia and, consequently, myopic anisometropia, which is more pronounced in urban areas.7,8,10 The present study did not prove whether the area of residence and the frequency of anisometropia are related. This parameter is highly dependent on the way in which each author classifies the area of residence, as rural or urban, and the limits of these regions are sometimes difficult to define. Also, living in a rural area and working in an urban area means that the daily experience of some populations turns out to be more urban, in both environments.
This study has several strengths. The study was carried out in children and adolescents in a school environment, which allows minimizing the potential bias that occurs in the sampling process and avoids overestimation of the problem when the investigation is carried out in a clinical environment. For this study, spherical anisometropia and astigmatic anisometropia were considered, the latter being disregarded in several studies and there is a record that this anisometropia is the one that most varies in terms of ethnicity.9

Certain limitations can be pointed out in this study. Firstly, the use of autorefraction without cycloplegia is highlighted, which is not the gold standard method of refraction. This fact limits the analysis of the distribution of the different types of refractive errors found in the population studied, because despite the use of an open field autorefractometer, recognized as an instrument with good agreement with cycloplegic retinoscopy and which eliminates the need for cycloplegia in children17,18 tends to underestimate hyperopia.17,19 However, for the present study, this situation does not weaken the conclusions, as the refraction was evaluated in an open field and binocularly, both eyes are exposed to the same conditions, in addition to that studies by other authors with the same methodology, point out a sensitivity 100% for the diagnosis of anisometropia.19 Secondly, the choice of the cut-off point for the classification of anisometropia is pointed out, which on the one hand, the literature recommends considering an IOD of at least 1.00D, the sensitivity studies of the autorefractometer used, recommend considering 1.25D.16 Thirdly, the signalling of the area of residence of the participants as rural or urban is reported, since the limits of these regions were at times difficult to define, noting also that being a study carried out in an area of the inner country, whose territorial classification is of low density, it is expectable that habits and behaviours are more uniform between rural and urban areas, than if the same study had been carried out in an area of greater population density.

Conclusions
The present study estimates the frequency of anisometropia in Portuguese children from preschool to the 3rd cycle of basic education finding an occurrence rate of 6.1%. The results of this work also show that the level of the study cycle and the spherical anisometropia are related, verifying that it is low in preschool education and higher in the 3rd cycle of basic education. It was also found that, hyperopic anisometropia is more frequent in younger children and that with the progress of the school path, myopic anisometropia predominates. Taking into account the high frequency of anisometropia found in 3rd cycle students, we are of the opinion that the performance of visual screening at this age is essential for the timely detection and correction of possible eye problems and that, consequently, will lead to better development, learning and school outcomes at these ages, which is why it is important to extend screening actions beyond childhood.

Data availability
Underlying data
Dryad: Portuguese Children Refractive data - VER+ Project, https://doi.org/10.5061/dryad.h4j0zpms5.27

This project contains the following underlying data:

- PortugueseChildrenRefractiveDataVERmaisProjectV2.xlsx

Data are available under the terms of the Creative Commons Zero “No rights reserved” data waiver (CC0 1.0 Public domain dedication).

Acknowledgments
To Rafaela Venâncio for the support and help in data collection. To the Vision Sciences Clinical and Experimental Centre and UBI medical for the availability of the equipment used and to the Beira Interior University Mission Group in Optometry and Vision Sciences for encouraging this study.

References


Open Peer Review

Current Peer Review Status: ? ?

Version 1

Reviewer Report 19 November 2021

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Pedro M. Serra
Research and Development Department, Ophthalmology Clinic Vista Sánchez Trancón, Badajoz, Spain

General comment

Thank you for considering my name as a reviewer of the manuscript titled “Frequency of anisometropia in children and adolescents”. I would like to congratulate the authors for their work in this field of vision sciences which has a special interest in countries where is a shortage of epidemiologic data in the field of vision.

Regarding the manuscript, my feeling is that it requires additional work before it is considered for indexing. In this report I will cover the technical issues that in my opinion would improve the quality of the manuscript, however, I would recommend the author’s linguistic editing of the final manuscript. Examples of linguistic improvement are very long sentences with multiple ideas and some lack of concise writing.

Specific topics

Abstract: Provide a statement defining the topic of research and a second sentence where you state the aim of the study (eg. This study aims to estimate the prevalence of anisometropia in the Portuguese population of children and adolescents.) I suggest changing the word frequency to prevalence throughout the text.

Methods:
  ○ Indicate the study design? (e.g. Observational Cross-sectional study)
  ○ How did you build the sample?
  ○ Describe the dependent and independent variables
  ○ Remove any data from the methods
Results
- Use direct messages (e.g. No association was found between the presence of anisometropia with gender or area of residence)

Conclusion
- The first sentence should be deleted this is not a conclusion from the present study.

Introduction:

I think the introduction requires some improvement
- 1st paragraph – Provides a definition of the research topic
  - “Anisometropia is an ocular disorder characterized by an interocular difference (IOD) in refractive error, representing a specific refractive condition insofar as the two eyes of an individual, with presumably similar sociodemographic, environmental and genetic influences, can have asymmetric eye growth." Please reformulate this sentence, particularly remove the word presumably.
  - 2nd paragraph and 3rd paragraph – mention the risk factors for anisometropia and the importance of assessing it
  - 4th paragraph- describes the instrument used. I would suggest moving this information to the methods
  - 5th paragraph- states the aim of the study.
  - Missing information- the authors should mention the prevalence studies published, especially in Portugal, and compare with other European countries.

Methods:

Please include:
- Type of study
  - Nature of the sample, how did you select the different groups? There are differences in the socioeconomic nature of the study sites? Please indicate how did you define Rural and Urban populations? (e.g. number of inhabitants covered by each school)?
  - Please indicate specifically the region where this study was conducted, this is important for instance in future meta-analysis studies.
  - Duration of the study (e.g September 2021 – November 2021)
  - Could you add information about the use of spectacles, you could try to see if the anisometropia had already been identified.

Instrument description
- Include PlusOptix manufacturer city and country
- Provide the repeatability of the instrument (published)

This is just a comment - “Students' data for which it was not possible to obtain refraction were excluded, due to technical issues associated with the performance of the instrument (presence of strabismus, opacities, retinal anomalies or when the refractive error exceeded the instrument's measurement limit - spherical measurement range or cylindrical from −7.00 to +5.00D) or due to lack of cooperation from the participant.”

This is probably one of the most valuable pieces of information from the data collection and it is a shame not being presented.

Data Analysis
- Please indicate how the reader can interpret Thibos' notation in regards to the J0 and J45.
- Say that the Cylinder component needs to be in negative form

Anisometropia Classification
- I suggest writing the formulas used for calculating the SA, MA, and sMA.

Statistical Analysis

Results
- Sample characterization – 1st paragraph move it to the methods section.

- Refractive State
  - Please provide a table or figure (Box plot) with the refractive error information, where is possible to see the mean, standard deviation and range
  - Figure 1 has limited information, I suggest including the percentages in the table mentioned above

- Anisometropia
  - Please, use written numbers when placing them at the beginning of a sentence. (e.g Forty-six not 46)
  - Provide information about the level of anisometropia per type. Describe the mean, standard deviation, and range
  - Suggest creating a figure (bar plot with the percentages of anisometropia, total, young age group and older age group)

Discussion
- The authors found a statistically significant association between the frequency of myopic anisometropia and age/ scholarly. Could the authors extend the discussion on the etiology of myopic anisometropia, which probably implies an asymmetric eye growth? Discussing this point could help the authors to suggest actions/mechanisms to prevent anisometropia.

- Discuss the consequences of hyperopic anisometropia, use the values (mean and standard
deviation) for arguing about the number of subjects in risk of developing amblyopia.

**Is the work clearly and accurately presented and does it cite the current literature?**
Partly

**Is the study design appropriate and is the work technically sound?**
Yes

**Are sufficient details of methods and analysis provided to allow replication by others?**
Partly

**If applicable, is the statistical analysis and its interpretation appropriate?**
Yes

**Are all the source data underlying the results available to ensure full reproducibility?**
Yes

**Are the conclusions drawn adequately supported by the results?**
Partly

**Competing Interests:** No competing interests were disclosed.

**Reviewer Expertise:** Vision Sciences, Ophthalmic Optics.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

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Carla Lança

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The study reports on the prevalence of anisometropia in a sample of Portuguese children and adolescents. The wording needs major revision. I have several comments as shown below.

**Title**
I suggest replacing the word “frequency” by “prevalence”. This suggestion also applies throughout all sections of the manuscript.

**Abstract**
- Methods - Please replace “cycloplegic” by “cycloplegia”.
- Results - Please revise the wording of the following sentence “to state that the occurrence...”; The last sentence of the results it's not clear and should be revised.

**Introduction**
- The first sentence is too long, and the wording needs to be revised. I suggest splitting it into two sentences. I have a similar comment for the third paragraph of the introduction section.
- There is no mention to previous studies on anisometropia prevalence. Also, there is the need to show more detailed results on the studies reporting risk factors and its association with anisometropia (e.g., sample size, age, p values, etc.).

**Methods**
- The methods section is incomplete. The methods section of a research paper provides the information by which a study's validity is judged. Therefore, it requires a clear and precise description of how an experiment was done, and the rationale for why specific experimental procedures were chosen. For example, more information is necessary on the sampling method and authors should describe their study design.

**Results**
- The first paragraph should be moved to the methods section.
- Table 2 – Replace “statistical test” by p value only (follow the same recommendation in the text results). Also, include a note referring to which comparisons are being made (for example, is it the distribution of children by cycles or the age by cycles?).
- At the time you are writing your article, you have already completed your study, so you should use past tense in your methodology and results section to record what you did and found (for example, “this difference was statistically significant”).
- Refractive state and anisometropia sections need to be re-written, as it is confusing to present two percentages at the same time. Perhaps the authors can consider showing separate sentences for those results.
- Influence of sociodemographic variables: the first sentence of this section should be moved to the statistical analysis; Delete “therefore this parameter is not in the table” and replace by the p value.
- Table 3 – delete the X2 value and only present p value. Non-significant p values may be presented with only 2 decimal places.
- For risk factor analysis the multivariate adjusted analysis should be additionally shown.
- Figure 2. The colour of the legend is not clear, and it is difficult to distinguish the categories presented in the graph. The y axis wording needs revision.

**Discussion**
- Please, delete the 1st sentence.
The differences between prevalence of anisometropia in Asia and Europe need a more careful explanation. Environmental factors play a major role in the development of refractive errors, especially myopia.

Another limitation of the study that was not referred is that factors such as reading habits or outdoor time were not collected and those may be risk factors for the development of refractive errors.

Is this the first study in Portugal? Are your results comparable with other studies in Portugal?

Conclusions

Please revise the wording on the sentence that includes the following: “we are of the opinion”.

Is the work clearly and accurately presented and does it cite the current literature?
Partly

Is the study design appropriate and is the work technically sound?
Partly

Are sufficient details of methods and analysis provided to allow replication by others?
Partly

If applicable, is the statistical analysis and its interpretation appropriate?
Partly

Are all the source data underlying the results available to ensure full reproducibility?
Yes

Are the conclusions drawn adequately supported by the results?
Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Refractive errors and strabismus

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.
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