



Faculté de Médecine et Pharmacie

ANNEE 2016

Thèse n°

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POUR LE DIPLOME D'ETAT
DE DOCTEUR EN MEDECINE
(décret du 16 janvier 2004)**

présentée et soutenue publiquement
le 30 Septembre 2016 à Poitiers
par Emilie Matamoros

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une analyse transversale**

COMPOSITION DU JURY

Président : Monsieur le Professeur Pierre Ingrand

Membres : Monsieur le Professeur Xavier Dufour
Madame le Docteur Michèle Boissonnot
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Le Doyen,

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INTRODUCTION

Myopia is an epidemic ocular disorder that has been increasing for the last 40 years.¹ Environmental risk factors for myopia have been extensively investigated. A high level of education and near-work activities have been associated with higher prevalence, whereas outdoor activities could have a protective effect.² Furthermore, different genetic factors with relatively small effect size have been reported in several genome-wide analyses, linkage analyses, and association studies in different populations, with more than 34 genes implicated in nonsyndromic myopia, most of them nonreplicated. These genes encode for various proteins located in extracellular matrix (collagen, fibromodulin, matrix metallopeptidase, catenin) or playing a role as growth factors (TGF-beta and hepatocyte growth factors) or as cholinergic and glutamate receptors.³ Eye growth and refractive development appear to be regulated by local signaling pathways within the eye from retina to sclera. Among different messenger molecules, experimental evidence supports the role of dopamine, which is released by dopaminergic amacrine cells, in the regulation of ocular axial growth and by consequence in the development of experimental myopia.^{4,5}

Epidemiological studies on REs have shown differences between ethnic groups. Caucasians seem to present higher prevalence rates for myopia compared to African or Hispanic individuals and the highest rate has been reported among Asians.⁶

For example, the rate of myopia was reported to be 95% in student population among Chinese university students in Shanghai in 2009 and 82% in a Singaporean study of military conscripts in 2010.⁷

In the Caucasian population, the prevalence of myopia reported varies according to country, with a rate of 15% in Australia in 1994 versus 26% in the USA in 1990.^{8,9} The present study aimed at evaluating the

prevalence of myopia in France in a large-scale clinical setting.

PATIENTS AND METHODS

Study Design

This study is a cross-sectional analysis of a large group of Caucasian individuals between January 2012 and November 2013, in 4 different eye treatment centers (2 in Paris, 1 in Lyon, and 1 in Bordeaux). These centers are especially dedicated to RE, and appointments are mainly given online.

The health interview and the visual examination were carried out by different physicians. They were started by orthoptists and pursued by ophthalmologists.

Data Collection

The data collected included age, gender, any relevant medical history such as laser refractive surgery, cataract surgery, peripheral laser photocoagulation for peripheral retinal tears, and retinal detachment. All individuals underwent an ophthalmic examination applying the same procedure, involving noncycloplegic autorefraction on both eyes in adults (Tonoref, Nidek) and cycloplegic autorefraction with cyclopentolate for children. Best-corrected visual acuity (BCVA) was assessed on a Monoyer chart, a visual acuity decimal scale, and determined after objective autorefraction and subjective refinement by ophthalmologists. A slit lamp examination was performed to assess lens status (cataract or clear lens, pseudophakic, aphakic).

Refractive Data

Myopia was defined as RE ≤ -0.50 diopters (D), mild myopia as RE comprised between -0.50 and -2.75 D, moderate myopia as RE comprised between -3.00 and -5.75 D, high myopia as RE of -6.00 or less and very high myopia as RE of -10 D or less. Hyperopia was

defined as RE $\geq +0.50\text{D}$ and emmetropia with RE comprised between -0.50 and $+0.50\text{D}$. Refraction measurements were converted into spherical equivalents, calculated as the spherical value plus half of the astigmatic value. For homogenous comparisons of eye refraction data, analyzes were conducted on the right eye only and based on the subjective refraction as previously published.

Exclusion criteria included previous laser refractive surgery or cataract surgery. There was no particular systemic disorder, by either ethnicity or age, for exclusion criteria. Patients with incomplete data on right eye were automatically excluded from the analysis by the software.

The study adhered to the tenets of the Declaration of Helsinki. Data were declared to the “Commission Nationale d’Informatique et Liberté” (CNIL numbers 1695933, 1633782, 1705829, 1730110) and anonymized for study purpose.

Statistical Analysis

Age and gender-specific prevalence of myopia, hyperopia, and emmetropia were assessed. Summary statistics are given as numbers (percentage). Statistical tests of homogeneity of prevalence across age groups and gender used the Chi-square test at the 5% significance level. Because of the correlation of measures performed on both eyes and to ensure statistical independence between observations, only right eyes were analyzed. As a control, we checked the absence of significant difference between right and left eyes in patients when data were available for the 2 eyes.

RESULTS

A total of 103,962 individuals were initially included in the study. Out of this initial group, 100,429 patients were finally included in the analysis. The relevant data are presented in the flow chart (Fig.1).

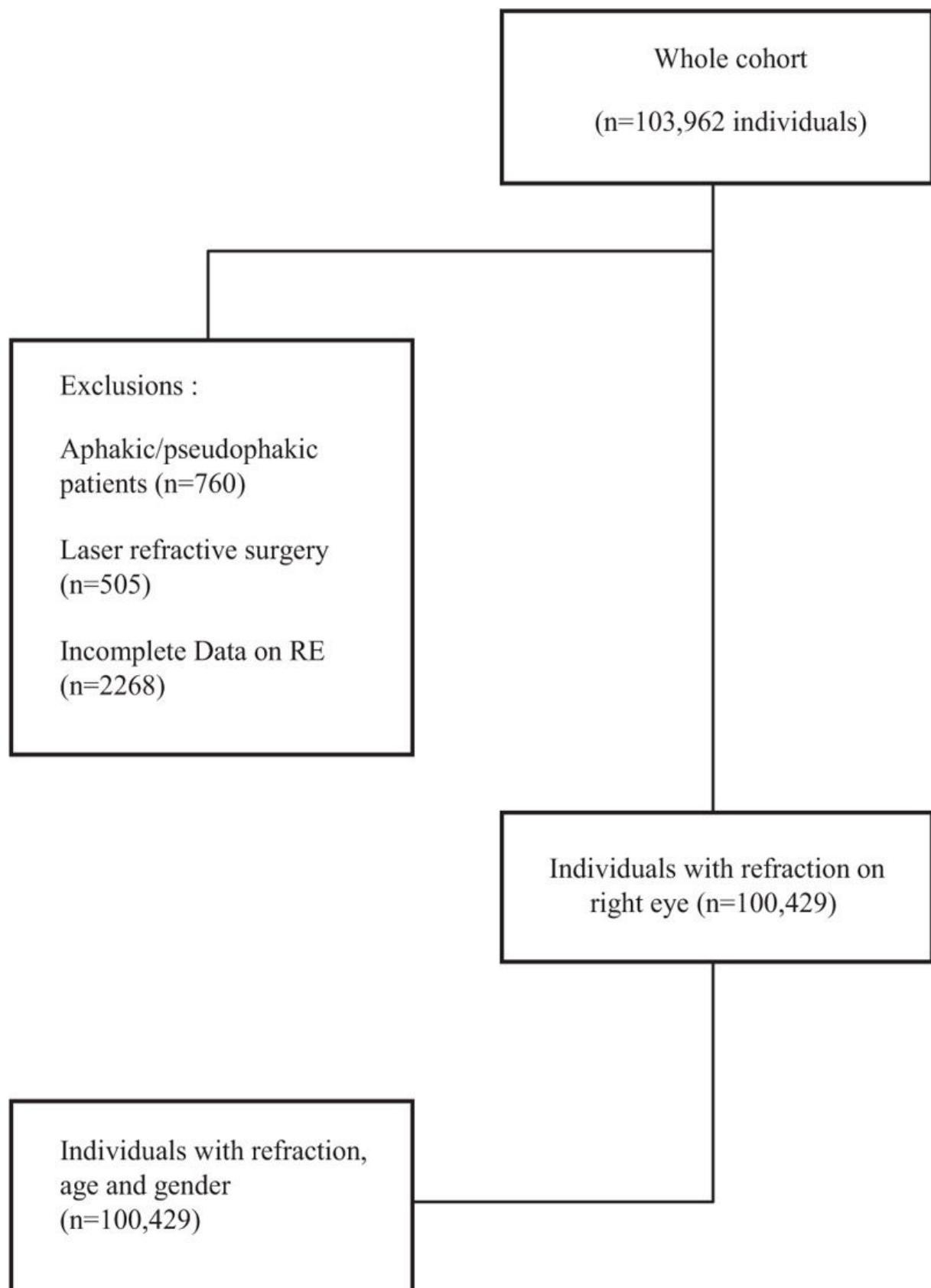


FIGURE 1. Flow chart of study patients.

The mean age (SD) of individuals was 38.5 years (± 16.9), with a sex ratio F/M of 1.39 (58,375 women /42,054 men).

The RE range varied from -27.50 to +20.25D, with a myopic shift more sizable than the hypermetropic shift. Figure 2 shows the distribution of RE on a semi-logarithmic scale in the whole series.

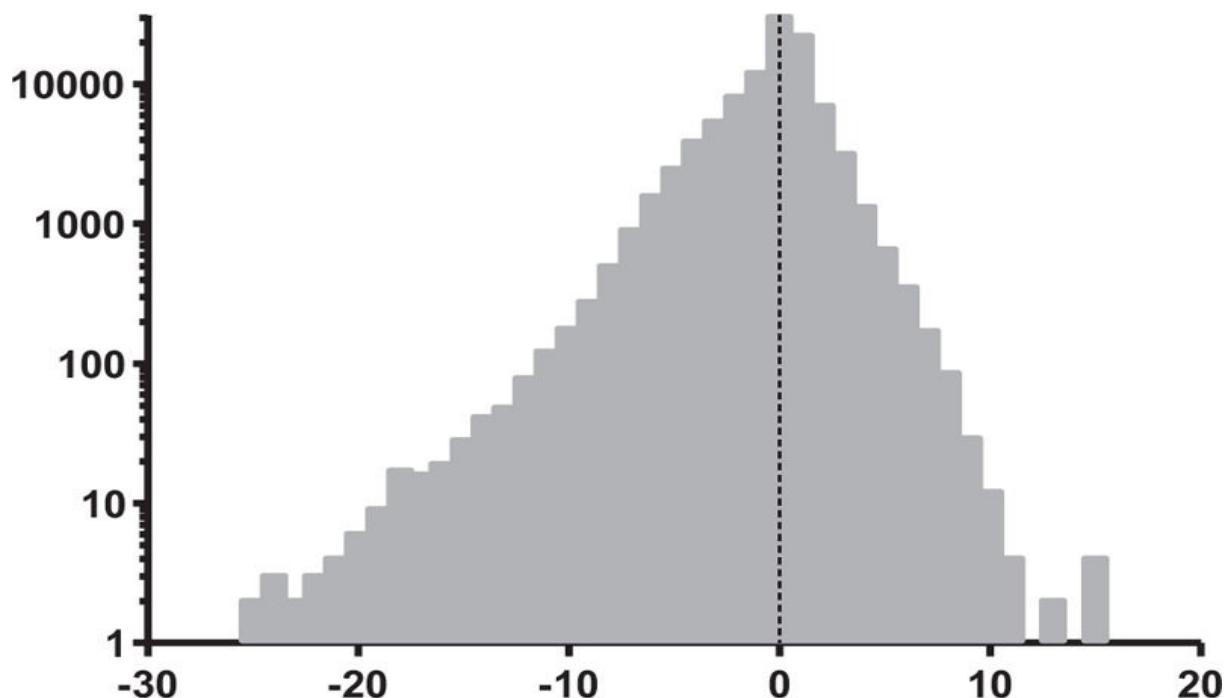


FIGURE 2. Distribution of refractive error on a semi-logarithmic scale in the whole series.

In this series, the overall prevalence of myopia was 39.1% (95% CI 38.8-39.4). The prevalences of mild, moderate, high and very high myopia were respectively 25.1% (95% CI 25.4-24.9), 10.6% (95% CI 10.4-10.8), 3.4% (95% CI 3.3-3.5) and 0.5% (95% CI 0.48-0.57).

Myopia and Age

The age-specific prevalence of myopia and high myopia were higher in the 20- to 39-year olds with a rate of 52.4% ($P<0.0001$) and of 4.4 % ($P<0.0001$) respectively. These data are more precisely indicated in Table 1.

Myopia and Gender

A total of 22,986 myopic women with a mean age of 33.5 (± 15.0) and of 16,295 myopic men with a mean age of 35.7 (± 14.4) were included. Prevalence of myopia was slightly higher in women than in men (39.4% vs. 38.8%). Gender comparison for myopia showed that the prevalences of mild, moderate, high, and very high myopia were significantly higher among women than among men. These data are presented in Table 1.

TABLE 1. Prevalence of Myopia: Age by Gender-Specific Data.

Age	No Myopia ≥ -0.5 D	Myopia ≤ -0.5D	Mild Myopia -0.5 to -2.75 D	Moderate Myopia -3 to -5.75 D	High Myopia ≤ -6 D	Very High Myopia ≤ -10 D		
							P (age)	P* (gender)
Both genders n (%)								
0 to 9	1197 (80.4)	292 (19.6)	264 (17.7)	25 (1.7)	3 (0.2)	0		
10 to 19	4753 (57.3)	3536 (42.7)	2575 (31.1)	813 (9.8)	148 (1.8)	24 (0.3)		
20 to 29	13655 (47.6)	15042 (52.4)	9525 (33.2)	4270 (14.9)	1247 (4.4)	129 (0.5)		
30 to 39	9238 (51.9)	8548 (48.1)	5346 (30.1)	2414 (13.6)	788 (4.4)	122 (0.7)		
40 to 49	11666 (68.9)	5269 (31.1)	3362 (19.9)	1394 (8.2)	513 (3.0)	93 (0.6)		
50 to 59	10527 (73.9)	3716 (26.1)	2300 (16.2)	1006 (7.1)	410 (2.9)	84 (0.6)		
60 to 69	6550 (77.4)	1908 (22.6)	1191 (14.1)	517 (6.1)	200 (2.4)	54 (0.6)		
70 to 79	2576 (80.0)	643 (20.0)	432 (13.4)	146 (4.5)	65 (2.0)	17 (0.5)		
≥ 80	986 (75.1)	327 (24.9)	255 (19.4)	62 (4.7)	10 (0.8)	3 (0.2)		
Total	61148 (60.9)	39281 (39.1)	25250 (25.1)	10647 (10.6)	3384 (3.4)	526 (0.5)		
P (age)		< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001		
Females n (%)								
0 to 9	1100 (81.2)	256 (18.9)	233 (17.2)	21 (1.6)	2 (0.2)	0		
10 to 19	3635 (59.8)	2448 (40.2)	1791 (29.4)	559 (9.2)	98 (1.6)	10 (0.2)		
20 to 29	8433 (48.1)	9116 (52.0)	5611 (32.0)	2702 (15.4)	803 (4.6)	85 (0.5)		
30 to 39	4938 (51.5)	4657 (48.5)	2765 (28.8)	1380 (14.4)	512 (5.3)	87 (0.9)		
40 to 49	6171 (68.4)	2658 (31.7)	1784 (19.8)	787 (8.7)	287 (3.2)	52 (0.6)		
50 to 59	5639 (73.3)	2052 (26.7)	1236 (16.1)	564 (7.3)	252 (3.3)	61 (0.8)		
60 to 69	3455 (77.1)	1025 (22.9)	626 (14.0)	284 (6.3)	115 (2.6)	35 (0.8)		
70 to 79	1413 (79.7)	359 (20.3)	245 (13.8)	74 (4.2)	40 (2.3)	11 (0.6)		
≥ 80	605 (73.8)	215 (26.2)	164 (20.0)	43 (5.2)	8 (1.0)	3 (0.4)		
P (age)		< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001		
Total	35389 (60.6)	22986 (39.4)	14455 (24.8)	6414 (11.0)	2117 (3.6)	344 (0.6)		
Males n (%)								
0 to 9	97 (72.9)	36 (27.1)	31 (23.3)	4 (3.0)	1 (0.8)	0		
10 to 19	1118 (50.7)	1088 (49.3)	784 (35.5)	254 (11.5)	50 (2.3)	14 (0.6)		
20 to 29	5222 (46.8)	5926 (53.2)	3914 (35.1)	1568 (14.1)	444 (4.0)	44 (0.4)		
30 to 39	4300 (52.5)	3891 (47.5)	2581 (31.5)	1034 (12.6)	276 (3.4)	35 (0.4)		
40 to 49	5495 (69.5)	2411 (30.5)	1578 (20.0)	607 (7.7)	226 (2.9)	41 (0.5)		
50 to 59	4888 (74.6)	1664 (25.4)	1064 (16.2)	442 (6.8)	158 (2.4)	23 (0.4)		
60 to 69	3095 (77.8)	883 (22.2)	565 (14.2)	233 (5.9)	85 (2.1)	19 (0.5)		
70 to 79	1163 (80.4)	284 (19.6)	187 (12.9)	72 (5.0)	25 (1.7)	6 (0.4)		
≥ 80	381 (77.3)	112 (22.7)	91 (18.5)	19 (3.9)	2 (0.4)	0		
P (age)		< 0.0001	< 0.0001	< 0.0001	< 0.0001	0.46		
Total	25759 (60.0)	16295 (38.8)	10795 (25.7)	4233 (10.1)	1267 (3.0)	182 (0.4)		
P* (gender)		0.34	< 0.0001	< 0.0001	< 0.0001	< 0.0001		

* Stratified Chi² Cochran-Mantel-Haenszel test (adjusted on age class).

DISCUSSION

This study reported a prevalence of myopia of 39.1% in a large French group of individuals for whom refractive data were collected in eye clinics dedicated to REs. Some Caucasian and Asian studies have shown similar prevalences, as did the American NHANE Study with 42.6% of myopia⁶ and the Japanese Tajimi study with a rate of 41.8%.¹⁰ The prevalences of myopia in the main studies of the last 30 years are presented in Table 2.

Myopia

In comparison with Asian studies, the prevalence of myopia in this French series was higher than the rates reported in the Handan Eye Study.¹¹⁻¹³ However, the prevalence remained lower than in the Korean NHNE Study.¹⁴ Other studies based on a Caucasian population have also reported lower prevalences.^{15,16} A recent European meta-analysis likewise estimated a lower prevalence of myopia with a rate of 30.6%.¹⁷ These lower prevalences might be due to our definition of myopia, as most of the other studies defined this condition as RE <-0.5D, while in our series myopia was defined as RE ≤-0.50D. Furthermore, when comparing the prevalence of myopia in our study to this last study (39.1% vs. 30.6%) it is important to note that the mean age of participants in both studies (38.5 years vs. 62 years in the European Eye Epidemiology Consortium) is likely to explain this apparent discrepancy. Indeed, the peak of myopia usually observed in younger participants, reaching 47.2% in those aged 25 to 29 years in the European Eye Epidemiology Consortium and 52.4% in those aged 20 to 29 years in our cohort, finally showing similar results.

It is worthwhile to note that the recent prevalence of myopia has increased when compared to studies performed over recent decades in different ethnic groups in Australia (15%), in the USA with the BDE Study

(26.2%), in Bangladesh (22.1%) and in China with the Beijing Study (22.9%) (Table 2).^{8,9,21,22}

Even if discrete, the prevalence of myopia was higher among women than men in the present study (Table 1). Different studies have demonstrated that, even in animal models, myopia was more prevalent in the female gender.^{23,24}

This difference could be due to hormonal factors as suggested in different studies.^{25,26}

If the pathophysiology of myopia has not been clarified to date, we now know that it implies a disruption of the emmetropization process and a dysregulation of the axial length control. Thanks to animal models, the molecular mediators implicated in this process have been partially identified, including vasoactive intestinal peptide, dopamine, retinoic acid, glucagon, insulin, γ -aminobutyric acid, transforming growth factor, basic fibroblast growth factor, and insulin-like growth factor-1.^{27,34} As a complex disorder with environmental and genetic risk factors involving many inheritance modes, myopia has been associated with 261 genetic disorders.³⁵

High Myopia

The prevalence of high myopia in different ethnic groups is also reported in Table 2. In this French national series, the rate of high myopia was lower to that reported in the Japanese Tajimi Study (3.4% and 8.2%, respectively) and similar than in the GHS Study (3.5%) and in a Korean Study (4%).^{9,14,16} This discrepancy may be due to differences in terms of recruitment. Indeed, in the Japanese Tajimi Study, high myopia was defined as -5D or less.

There is a lack of data on prevalence of myopia in the young population, mainly in Europe. Indeed, the most recent European studies reported values for older people aged 35 to 74 years or 44 to 78 years.^{16,17} In our

study, when focusing on the prevalence of myopia in the 10- to 39-year range, we observed a rate of 49.5%. This prevalence was clearly inferior to the prevalence reported in the same population group in the Korean Study (75.1%).¹⁴

TABLE 2. Prevalence of High Myopia in Different Ethnic Groups.

Studies	Year	Number	Mean Age	Cycloplegia	Overall Myopia <-0.5 D (%)	High Myopia (%)
Caucasian Studies						
Beaver Dam Eye study ⁹	1988–1990	4275	43–84	No	26.2	—
Blue Mountains Eye Study ⁸	1992–1994	3654	43–54	No	42.9	—
NHANES ⁶	1999–2004	12,010	20–39	No	15	—
EPIC-Norfolk Eye Study ¹⁵	2010	2519	40–59	No	50.2	7.4 (<-5 D)
The Gutenberg Health Study ¹⁶	2007–2012	13,959	≥60	No	50.1	7.8 (<-5 D)
European Eye Epidemiology Consortium ¹⁷	1990–2013	61,946	35–74	No	26.5	3.1 (<-5 D)
French National Study	2012–2013	102,705	44–78	No	27	—
Asian/Indian studies						
Pakistani Study ¹⁸	2002–2003	14,490	10–40	No	36.5	4.6 (<-5 D)
Andhra Pradesh Eye Disease Study ¹⁹	1996–2000	10,293	40+	No	34.6	4.5 (<-5 D)
Taiwan Study: Shihpai Eye Study ²⁰	1999–2000	1108	65	No	18.3	2.3 (<-6 D)
Bangladesh ²¹	2004	11,624	30	No	22.1	1.8 (<-5 D)
Beijing China ²²	2005	4439	40–101	-	22.9	2.6 (<-6 D)
Singapore Malay Eye Study ¹¹	2004–2006	2974	40–80	No	30.7	—
Liwan Eye Study ³⁶	2006	1405	50+	No	32.3	—
Handan Eye Study ¹³	2006–2007	6491	30+	-	26.7	1.8 (<-5 D)
Tajimi Study ¹⁰	2008	3021	40+	No	41.8	8.2 (<-5 D)
Singapore Indian Eye Study ¹²	2007–2009	3400	40	No	28	4.1 (<-5 D)
Chinese University Students ⁷	2009	5083	18–24	No	95.5	19.5
KNHNS ¹⁴	2008–2011	14,285	40–50	No	34.7	4 (<-6 D)
Singapore Military Conscripts ³⁷	1996–1997	22,562	20–79	No	48.1	—
	2009–2010	15,085	16–25	No	79.2	13.1 (<-6 D)
National Survey Taiwanese school children ³⁸	2000	28,908	17–29	No	81.6	14.7 (<-6 D)
Yes	10,889	16–18	Yes	84	21	21 (<-6 D)
African studies						
Barbados Eye Study ³⁹	1999	4036	40–84	No	21.9	—
NHANES ⁶	1999–2004	2343	20–39	No	49	5.5
U.S. Blacks			40+	No	36.5	4.3

Most studies demonstrate an increase in the prevalence of myopia among younger urbanized individuals with generally higher myopia rates and longer axial length than in older individuals.⁴⁰ This trend is likely to be explained by the environmental risk factor entailed by more near-work activities and fewer outdoor activities, both of which are frequently associated with a young urbanized and educated population.⁴¹ Conversely, the lower prevalence of myopia in rural population areas is likely to be due to reduced exposure to these factors.

LIMITATIONS

The present study was not designed to assess the risk factors of myopia, because our main objective was to measure the prevalence of myopia in different population age groups, and not to focus on epidemiological risk factors that had previously been extensively studied.^{14,15,41} For this reason, we did not correlate prevalence of myopia to educational level or to other environmental factors.

We also acknowledge that the prevalence of myopia may have been underestimated in our study, by exclusion of pseudophakic individuals and refractive surgeries, but because the vast majority of our patients did not undergo refractive or cataract surgery, unshown data including these factors did not influence the overall prevalences of myopia and high myopia. On the other hand, because refractive data are not extracted from the general French population, our approach may overestimate the prevalence of myopia in individuals aged less than 50 to 55 years old, because people with no RE are less likely to make an appointment than people with RE. However, in groups aged 50 and more, our refractive data are likely to be comparable to those of the general French population because appointment for refraction is then required in case of presbyopia. Moreover, the prevalence of myopia observed in our study

results is similar to a nationally representative sample of the US population (NAHNES, n=12,010 individuals) and to the European Eye Epidemiology (E3) Consortium (n=61,946 individuals).^{6,17}

Cycloplegia was not used systematically for adults, as it would have been considered unusual given the fact that in most studies on the same topic, it is not administered. Indeed, in a study including more than 2500 adult participants, the mean difference in spherical equivalent between measurements before and after cycloplegia was 0.29D. The difference was greater among young persons with hyperopic REs.⁴² Considering children, the refractive data can be considered as reliable because cycloplegia with cyclopentolate was systematically used before refraction assessment.

This is to our knowledge one of the largest group of European individuals dedicated to REs. On this topic, international consortia involving a large number of individuals have focused on genetic factors of myopia, with the results of their studies published in a number of top-ranked journals.⁴³ Given the complexity of myopic disease, in which genetic variants as well as environmental factors require careful consideration, there is a need for collaboration between different specialists in view of determining and depicting their respective causative effects.

Finally, regarding the high prevalence of myopia in our population, we cannot clearly confirm the hypothesis of a generally lower prevalence of myopia in European adults compared to Asian population.

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ABSTRACT

Refractive error (RE), particularly myopia, is the first cause of visual impairment throughout the world. This study aimed to depict the prevalence of myopia in a multicentric series of French individuals.

This cross-sectional analysis was carried out between January 2012 and November 2013 in eye clinics dedicated to REs. Data collection included age, gender, best-corrected visual acuity, RE, and any relevant medical history involving laser refractive surgery and cataract surgery. Exclusion criteria consisted of monophthalm patients or those with incomplete demographic data.

Prevalences in the overall population, by gender and by age groups were reported for mild myopia (-0.50 to -2.75 diopter [D]), moderate myopia (-3 to -5.75 D), high myopia (less than -6 D), and very high myopia (less than -10 D).

The analysis included 100,429 individuals, mean age 38.5 years (± 16.9). Overall prevalence of myopia was 39.1% (95% CI 38.8-39.4). Prevalences of mild, moderate, high and very high myopia were respectively 25.1% (95% CI 25.4-24.9), 10.6% (95% CI 10.4-10.8), 3.4% (95% CI 3.3-3.5) and 0.5% (95% CI 0.48-0.57).

Even if possible bias occurred in recruitment, our results are similar to RE data collected in nationally representative samples of Caucasians in other studies. This is to our knowledge, one of the largest European series of individuals dedicated to myopia prevalences in different age groups. These results confirm the importance of myopia as a major health issue in Western countries.

Abbreviations: CI = confidence interval, D = diopter, RE = refractive error.

Key words: epidemiology; myopia; high myopia; pathologic myopia; axial myopia; refractive error.



OBSERVATIONAL STUDY

OPEN

Prevalence of Myopia in France *A Cross-Sectional Analysis*

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SERMENT



En présence des Maîtres de cette école, de mes chers condisciples et devant l'effigie d'Hippocrate, je promets et je jure d'être fidèle aux lois de l'honneur et de la probité dans l'exercice de la médecine. Je donnerai mes soins gratuits à l'indigent et n'exigerai jamais un salaire au-dessus de mon travail. Admis dans l'intérieur des maisons mes yeux ne verront pas ce qui s'y passe ; ma langue taira les secrets qui me seront confiés, et mon état ne servira pas à corrompre les mœurs ni à favoriser le crime. Respectueux et reconnaissant envers mes Maîtres, je rendrai à leurs enfants l'instruction que j'ai reçue de leurs pères.

Que les hommes m'accordent leur estime si je suis fidèle à mes promesses ! Que je sois couvert d'opprobre et méprisé de mes confrères si j'y manque !



RESUME

L'erreur réfractive (ER), notamment la myopie, est la première cause de déficience visuelle dans le monde. Cette étude visait à décrire la prévalence de la myopie dans une cohorte multicentrique de personnes françaises.

Cette analyse transversale a été réalisée entre Janvier 2012 et Novembre 2013 dans des centres ophtalmologiques dédiés aux ER. Le recueil de données comprenait l'âge, le sexe, la meilleure acuité visuelle corrigée, l'ER, et les antécédents médicaux pertinents impliquant la chirurgie réfractive au laser et la chirurgie de la cataracte. Les patients avec des données réfractives ou démographiques incomplètes étaient exclus.

Les prévalences de la myopie pour l'ensemble de la population à l'étude, étaient analysées selon le sexe et l'âge, pour la myopie légère (-0,50 à -2,75 dioptres [D]), la myopie modérée (-3 à -5,75 D), la myopie forte (moins de -6 D), et la myopie très forte (moins de -10 D).

L'analyse a inclus 100 429 individus, l'âge moyen était de 38,5 ans ($\pm 16,9$). La prévalence globale de la myopie était de 39,1% (IC 95% 38,8-39,4). Les prévalences de myopie légère, modérée, forte et très forte étaient respectivement de 25,1% (IC 95% 25,4-24,9), 10,6% (IC 95% 10,4-10,8), 3,4% (IC 95% 3,3-3,5) et 0,5% (IC 95% 0,48-0,57).

Même si de possibles biais de recrutement ont existé, nos résultats sont semblables aux ER recueillies dans d'autres études aux échantillons nationaux représentatifs de Caucasiens. Ceci est à notre connaissance, une des plus grandes séries européennes dédiées à la prévalence de la myopie dans des groupes d'âge différents. Ces résultats confirment l'importance de la myopie comme problème de santé publique dans les pays occidentaux.

Mots clés: épidémiologie; myopie forte; myopie pathologique; myopie axiale; erreur réfractive.