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Article

Estimating the Genetic Contribution to Astigmatism and Myopia in the Mexican Population

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Abstract

Astigmatism and myopia are two common ocular refractive errors that can impact daily life, including learning and productivity. Current knowledge suggests that the etiology of these conditions is the result of a complex interplay between genetic and environmental factors. Studies in populations of European ancestry have demonstrated a higher concordance of refractive errors in monozygotic (MZ) twins compared to dizygotic (DZ) twins. However, there is a lack of studies on genetically informative samples of multi-ethnic ancestry. This study aimed to estimate the genetic contribution to astigmatism and myopia in the Mexican population. A sample of 1399 families, including 243 twin pairs and 1156 single twins, completed a medical questionnaire about their own and their co-twin's diagnosis of astigmatism and myopia. Concordance rates for astigmatism and myopia were estimated, and heritability and genetic correlations were determined using a bivariate ACE Cholesky decomposition method, decomposed into A (additive genetic), C (shared environmental) and E (unique environmental) components. The results showed a higher concordance rate for astigmatism and myopia for MZ twins (.74 and .74, respectively) than for DZ twins (.50 and .55). The AE model, instead of the ACE model, best fitted the data. Based on this, heritability estimates were .81 for astigmatism and .81 for myopia, with a cross-trait genetic correlation of $rA = .80$, nonshared environmental correlation $rE = .89$, and a phenotypic correlation of $rP = .80$. These results are consistent with previous findings in other populations, providing evidence for a similar genetic architecture of these conditions in the multi-ethnic Mexican population.

Keywords: Astigmatism; Myopia; Mexican population; Genetics; Twin studies

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Astigmatism and myopia are two prevalent ocular refractive errors that have become significant public health concerns globally (Baird et al., 2020; Hashemi et al., 2017; Pascolini & Mariotti, 2012). Astigmatism is characterized by unequal curvatures in the cornea or crystalline lens, leading to rotational asymmetries and blurry projections of light over the retina (Harb & Wildsoet, 2019; Harris, 2000; Visnjić et al., 2012). Myopia, also known as nearsightedness, is caused by the light being focused in front of the retina instead of on it, leading to a blurred perception of distant objects (Harb & Wildsoet, 2019). The elongation of the eye and corneal modifications (e.g., keratoconus) can contribute to myopia (Baird et al., 2020).

The worldwide prevalence of myopia was estimated to be ~33% by the World Health Organization in 2020, and a meta-analysis of global studies estimated a prevalence of 26.5% for myopia and 40.4% for astigmatism (Holden et al., 2016). However, data varies greatly between regions and ethnic groups, with higher prevalence in some groups (Hashemi et al., 2017; Rose et al., 2001). For example, in East and Southeast Asia, myopia is considered an epidemic among adults, with 80–90% suffering from it (Morgan et al., 2018). In contrast, half of the European population suffer from some refraction error, with around 30% of myopia and 23% of astigmatism (Williams et al., 2015). The comorbidity between astigmatism and myopia also varies among populations; for example, it has been estimated at 3.8% (3250/19,686) in the

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Albanian population (Kleves, 2021), but at 58% in American children (Fulton et al., 1982). Meanwhile, data from other regions, such as Latin America, is scarce. In Mexico, astigmatism and myopia have been recognized as common ocular problems (Secretaría de Salud, 2020). Specifically, in a sample of 676,856 Mexican patients (aged 6 to 90), myopia was the most common refractive error at 24.8%, while astigmatism was present in 13.5% of the sample (Gomez-Salazar et al., 2017). Studies of school-age children in urban areas showed a prevalence of 44% for bilateral myopia and 9.5% for astigmatism, while those in rural areas were estimated at 9.7% and 4.4% respectively (Garcia-Lievanos et al., 2016). Refractive errors impact aspects of life such as education and employment (Kandel et al., 2017); as such, the concern about these conditions is growing. They are predicted to affect over 50% of the world's population by 2050 (Holden et al., 2016); thus, evaluating the etiology of refractive errors is crucial.

Previous research suggests that both genetic and environmental factors play a role in the development of astigmatism and myopia (Baird et al., 2020; Gordon-Shaag et al., 2021; Read et al., 2007; Young et al., 2007). For instance, genomewide association studies (GWASs) have identified various risk polymorphisms for both conditions, including genes involved in eye growth, retinal proteins, corneal epithelium, neurotransmission, and retinoic acid metabolism (Harb & Wildsoet, 2019; Hysi et al., 2010; Kiefer et al., 2013; Lopes et al., 2013; Nakanishi et al., 2009; Shah, Li et al., 2018; Wojciechowski, 2011; Wojciechowski & Hysi, 2013). However, the genetic connection between astigmatism and myopia remains inconclusive, with some studies suggesting a shared genetic etiology (Pinazo-Durán et al., 2016; Shah, Guggenheim et al., 2018; Young et al., 2007) and others considering them as different manifestations of refractive errors (Dirani et al., 2008; Hammond et al., 2001; Paget et al., 2008). Environmental factors, such as prolonged near-work activities, outdoor time, reduced sleep, education, muscle changes, and population density also seem to play a role (Demir et al., 2021; Harb & Wildsoet, 2019; Li et al., 2019; Saad & El Bayoumy, 2007; Wang et al., 2021; Wojciechowski, 2011; Xiong et al., 2017; Zhang et al., 2010). For example, studies have suggested that more time spent in outdoor activities reduces the risk of developing myopia (Jin et al., 2015; Xiong et al., 2017); meanwhile, near-work activities such as reading or the overuse of smartphones, which involve short viewing distance, force the eye to modify the optical convergences and increase eyelid pressure onto the cornea, resulting in increased risk of developing both myopia and astigmatism (Dutheil et al., 2023; Leung et al., 2020). Other studies have suggested that sociodemographic variables could be related to developing myopia, as this is more prevalent in urban and higher income populations compared to rural and lower income, which could be related in turn to near-work and outdoor activities (Ragot et al., 2020).

Twin studies are useful in evaluating the combined impact of genes and environment (Sahu & Prasuna, 2016). For example, a study in Norway showed higher concordance rates for astigmatism in monozygotic twins than in dizygotic twins, suggesting a genetic influence (Grjibovski et al., 2006). The heritability of astigmatism was estimated to be over 60% in an Australian twin study (Dirani et al., 2008). In addition, a Chinese twin study also found significant contributions from both genes and environment to myopia (C.-J. Chen et al., 1985). However, the contribution of genes and environment in genetically admixed populations, such as the Mexican, is practically unknown. The Mexican population is largely underrepresented in genetic studies but has a high prevalence of refractive errors. This study aims to determine the concordance rates, heritability, and genetic cross-trait correlation of astigmatism and myopia in Mexican twins.

Methods

Sample

Data used for this study comes from the Mexican Twin Registry, TwinsMX (https://twinsmxofficial.unam.mx/; Leon-Apodaca et al., 2019), collected using the Research Electronic Data Capture (REDCap) platform, hosted at the National Laboratory of Advanced Scientific Visualization at the Universidad Nacional Autónoma de México (UNAM). All participants gave informed consent, and the study protocol was reviewed and approved by the Research Ethics Committee of the Institute of Neurobiology at UNAM.

At the time of data extraction (April 2022), TwinsMX included data for 2778 families. For this study, we selected subjects who completed the medical questionnaire and were aged 7 years or older (considering that the age to start school can vary between 6−7 years old in Mexico), resulting in a sample of $N = 1887$ families. Zygosity status was participant-reported; twin pairs whose reported zygosity did not match (e.g., one twin reported MZ and the co-twin reported DZ) were classified as indeterminate (Sánchez-Romera, 2013) and were excluded ($n = 9$). Subjects from other multiple birth types (e.g., triplets or quadruplets) or who did not report the sex of their co-twin were also excluded. The final sample consisted of $N = 1399$ families. A family was defined for either a singleton or a pair of twins. In this study, 243 families with both twins being registered (i.e., 486 individuals) and 1156 families with only one registered twin were included in the final sample. The 1156 single twins reported information about their unregistered twin, and with this information we were able to analyze a sample of $N = 2798$ individuals (i.e., 486 + [1156*2]). Sociodemographic data, sex and age of the twins were also acquired.

Myopia and Astigmatism Participant-Reported Diagnosis

Twins answered a medical questionnaire where they were asked 'Have you, your parents, siblings, or children ever suffered some of the following conditions?', and tick boxes allowed participants to state which family members had presented with the condition. Among the possible answers, myopia and astigmatism were listed.

Statistical Analyses

Participants were split into two main groups, All MZ and All DZ, based on the self-reported zygosity. Additionally, each twin reported their sex and their twin's sex. With that information, families were classified into five different subgroups depending on zygosity and sex as has been widely reported: MZ female (MZF), MZ male (MZM), DZ female (DZF), DZ male (DZM), and DZ opposite-sex (DZOS) (e.g., Grjibovski et al., 2006; Hopper et al., 1990; Loat et al., 2004; Vink & Boomsma, 2011).

The participant-report diagnosis was used for families where both twins were part of the registry. For the families where only one of the twins was part of the registry (single twins), we considered the report about themselves and the report about their twin. To address the concern of reliability of a single twin reporting the diagnosis of the nonregistered co-twin, we adopted the following strategy: first, we analyzed the responses from the 243 twin pairs (both twins registered) and tested the consistency of their answers regarding their co-twin. That is, we compared the twins' response

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about their co-twin, since in these 243 families we have data from both twins.

In addition, we estimated the concordance rate for the diagnoses (i.e., presence or absence of astigmatism and myopia, independently performed one from another) only for the 243 twin pairs, to assess whether the results obtained from the entire sample (i.e., 1399 families) were consistent.

Demographic analysis. We compared the distribution of sex and age between the MZ and DZ groups using an independent chi-square test (χ^2). Additionally, we reported the prevalence of having at least one of the two conditions, that is, only myopia, only astigmatism, or both. We used an independent chi-square test to evaluate whether sex or zygosity distribution differed among the three groups.

Concordance rate test. We calculated probandwise concordance for both astigmatism and myopia following the model reported by McGue (1992), and calculated the respective confidence intervals for proportions for each group and subgroups of zygosity and sex. Due to the small sample size of some of the zygosity and sex subgroups, only the comparisons between concordance rates for All MZ and All DZ groups, without stratification by sex, were tested with the Likelihood Ratio Test. Only results with $p < .05$ were considered statistically significant.

Bivariate ACE Cholesky analysis. We performed the ACE Cholesky decomposition, which allows estimating the amount of variance of each phenotype, explained by the genetic contribution or heritability (A), the shared environmental contribution (C), and the unique environment (E). In addition, a multivariate design (in this case, a bivariate model) allows to estimate the covariation between myopia and astigmatism. For a detailed description of these analyses, see Zietsch et al. (2014) and Posthuma (2009).

Briefly, the bivariate model assumes that latent variables have effects on the traits of interest (see Figure 1 for the path model). First, we consider the genetic contribution from two sets of genes (latent variables A1 and A2) by directly associating the first gene set over one trait (i.e., A1 over astigmatism) through a path (a_{11}), and the second set of genes over the second trait (i.e., A2 acting over myopia) through a second path (a_{22}). Second, the model takes into account the shared genes for astigmatism and myopia, which are modeled on the influence of A1 over the second trait, myopia (path a_{21}). The effect of the set of genes A2 over the first trait (astigmatism) via a_{12} is not modeled to avoid redundancy; namely, it is assumed that if an overlapping of shared genes exists, these will be the same group of genes within A1 or A2 sets, then the path a_{21} is already reflecting the conjunction of shared genes. Additionally, it is relevant to notice that, in a Cholesky factorization, the lower triangular solution is mathematically equivalent to the upper triangular solution (see matrix *a* below). Similarly, the respective shared and nonshared environmental contributions are correspondingly modeled by C and E from paths.

The corresponding matrix design of this bivariate path model is an $n \times n$ matrix, where n is the number of traits in the model, in this case, a 2 × 2 matrix $a = \begin{pmatrix} a_{11} & 0 \\ a_{21} & a_{22} \end{pmatrix}$. The total genetic contribution is estimated as the result of $A = a*a^T$, given as a result $A = \begin{pmatrix} a_{11}^2 & a_{11}a_{21} \\ a_{21}a_{11} & a_{21}^2 a_{22}^2 \end{pmatrix}$. The $A(1,1) = a_{11}{}^2$ is the total genetic contribution (i.e., heritability) of the trait 1, $A(2,2) = a^2{}_{21} + a^2{}_{22}$, is the total genetic contribution (i.e., heritability) of the trait 2. Meanwhile, the cross-trait, cross-twin genetic covariance is $A(2,1) = a_{11}a_{21}$. To estimate the genetic correlation between the traits of interest, astigmatism, and myopia, $r_A = \frac{a_{11}*a_{21}}{\sqrt{a_{11}^2} * \sqrt{a_{21}^2 + a_{22}^2}}$. The variance and covariance matrices, and correlations for C and E can be calculated analogously.

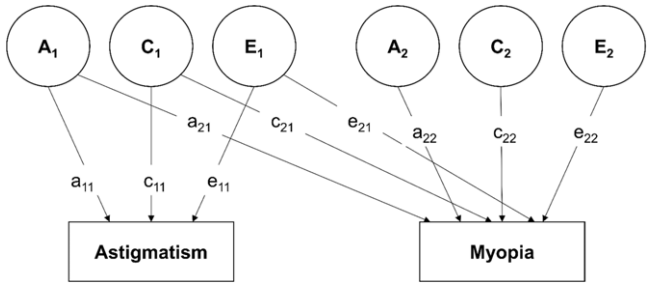

Figure 1. Bivariate path modeling for astigmatism and myopia. Cholesky decomposition in latent variables: A (genetic contribution), C (shared environment influence), and E (residual or nonshared environmental influences). A1 represents the latent variable (i.e., the set of genes) that contributes to astigmatism (path a11) and myopia (path a21). A2 is the second latent variable (i.e., a second set of genes) affecting myopia. Also shown are the respective variables for shared and nonshared environmental contributions (C and E).

Data analysis was performed in Ubuntu 22.04 using RStudio v.4.2.0 (2022-04-22, SCR_000432), and packages — tidyverse (v.1.3.1, Wickham et al., 2019, SCR_019186), gt (v.0.6.0, Iannone et al., 2022) and the UMX package, (v.4.10.50 and OpenMx v2.20.6) (Bates et al., 2019) — were used for the bivariate structural modeling of the ACE Cholesky decomposition. For the umxACE function, the arguments addCI and Intervals were set up as True; the modeling was performed using the 'CSOLNP' optimizer. All code is available in GitHub URL: https://github.com/NeuroGenomicsMX/TwinsMX_Astigmatism_Myopia.

Results

Considering that DZ twin pairs can be discordant for sex, we performed a chi-square test between MZ and DZ twins for the total sample by sex. The chi-square test did not show significant differences in sex ratios between DZ and MZ, $\chi^2(1, N = 2798) = 1.83$, $p = .18$. Figure 2 shows subgroups or pairs segregated by zygosity and sex (2A) and distribution by age group (2B). No differences in distribution by age group were observed between MZ and DZ pairs, $\chi^2(4, N = 1399) = 7.1623$, $p = .13$.

The prevalence of astigmatism, myopia, and their comorbidity —that is, their co-occurrence — were characterized in the whole sample. Considering the whole sample, 50.90% (1424/2798) of the individuals had at least one of the two diagnoses (astigmatism or myopia). Specifically, 5.5% (155) of the individuals were diagnosed only with astigmatism, 14.58% (408) only with myopia, and 30.77% (861) were diagnosed with both. There were no differences between the distribution of these three groups by zygosity, MZ versus DZ, $\chi^2(2, n = 1424) = 2.21$, $p = .33$, nor by sex, $\chi^2(2, n = 1424) = 0.23$, $p = .89$; see Figures 3A and 3B respectively.

Astigmatism. Among 1399 families, the prevalence of astigmatism was 36% (1016/2798). Concordance rates results showed that MZ twins had a significantly higher astigmatism concordance than DZ, .74 versus .50; $\chi^2(1) = 40.20$, $p = 2.29 \times 10^{-10}$ (Table 1).

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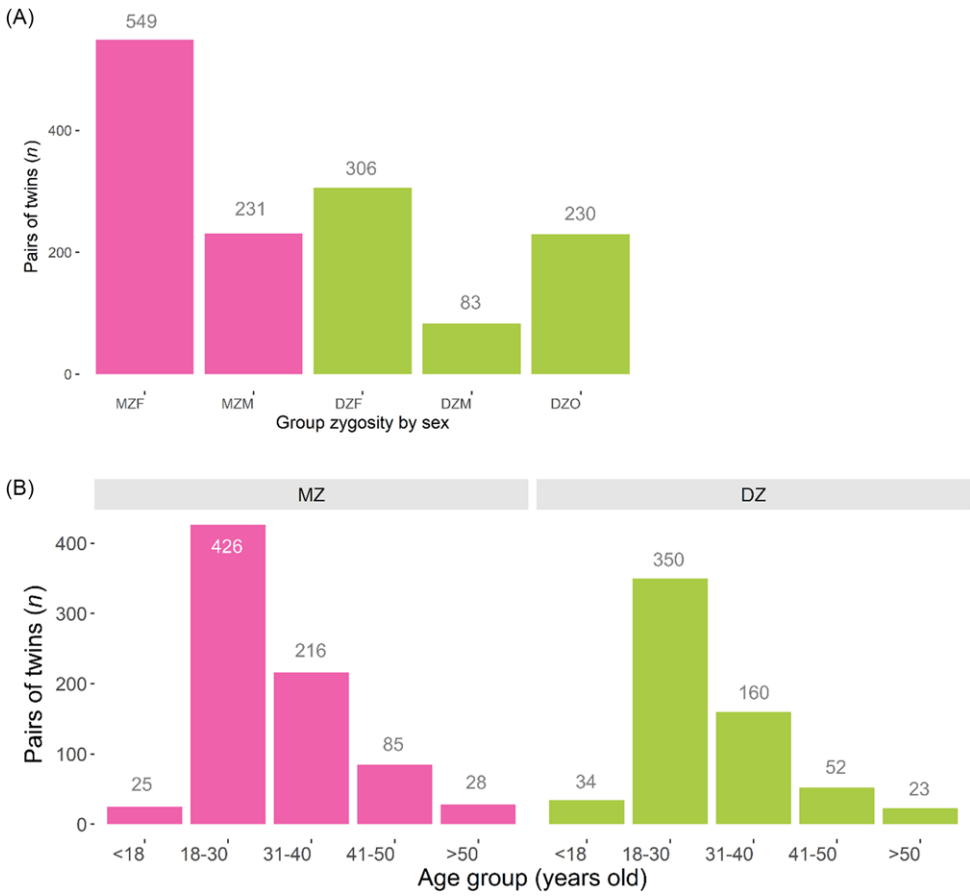

Figure 2. A. Twin pairs segregated by zygosity and sex. No differences by group were observed (p = .18). B. Twin pairs segregated by zygosity and age group. No differences between DZ and MZ pairs were observed (p = .13).
Note: MZ, monozygotic; DZ, dizygotic; MZF, MZ female; MZM, MZ male; DZF, DZ female; DZM, DZ male; DZO, DZ opposite sex.

Myopia. The prevalence of myopia was 45% (1269/2798). The concordance rate was significantly higher for MZ than for DZ twins, .74 versus .55, $\chi^2(1) = 33.09$, $p = 8.80 \times 10^{-9}$ (Table 2).

Additional Analysis for Complete Pairs Only

The same statistics were estimated for the subsample that included the participant-report of both twins (243 pairs). Consistent with the previous results (considering the report from one twin about both twins), MZ twins showed higher concordance rates for astigmatism, $\chi^2(1) = 14.72$, $p = 1.20 \times 10^{-4}$ (Table 3) and myopia, $\chi^2(1) = 12.08$, $p = 5.0 \times 10^{-4}$ (Table 4).

Heritability and Cross-Trait Correlation

The Akaike information criterion (AIC) showed that the AE model had a better fitting that the ACE model (Table 5). The estimates and their corresponding 95% CI for ACE and AE are detailed in Figure 4.

The additive genetic effects or heritability (A) for astigmatism (a^2_{11}) was estimated at .81 (95% CI [.74, .82]) with residual or nonshared environmental contributions (e^2_{11}) E = .19 (95% CI [.17, .25]). Meanwhile, heritability ($a_{21}{}^2 + a_{22}{}^2$) for myopia was estimated at A = .81 (95% CI [.73, .89]) and E ($e_{21}{}^2 + e_{22}{}^2$) = .19 (95% CI [.15, .21]). Additionally, bivariate modeling allowed us to estimate the cross-trait correlation; for this model the genetic correlation was rA = .80 (95% CI [0.77, 0.83]), and nonshared environmental correlation rE = .89 (95% CI [0.84, 0.91]). Finally, the phenotypic correlation between astigmatism and myopia due to additive genetic influences was rP = .79 (95% CI [.76, .82]), and the phenotypic correlation due to nonshared environmental influences was estimated at .21 (95% CI [.18, .24]). The calculations for these bivariate effects and cross-trait correlations are carefully detailed in (Munn et al., 2010).

Discussion

This study aimed to estimate the concordance rates and heritability of myopia and astigmatism in Mexican twins. Given the genetically diverse ancestral composition of the Mexican population (García-Ortiz et al., 2021; Martínez-Cortés et al., 2012), this study is relevant to better understand the relevance of genes on these diagnoses in genetically admixed populations that are typically underrepresented in research. The results showed higher concordance rates for myopia and astigmatism in monozygotic (MZ) twins compared to dizygotic (DZ) twins. The estimated heritability was .81 for each of the traits, astigmatism and myopia, and the genetic correlation (rA = .80) suggests that both traits are influenced by a shared set of genes.

Although a correlation lower than one does not necessarily imply that the set of shared genes has a similar effect on both astigmatism and myopia (Posthuma, 2009), the high value of the genetic correlation in this study supports the conclusion that astigmatism and myopia share a genetic basis and overlap in their genetic effects. Accordingly, a genomewide association study (GWAS) in a sample with European ancestry found that the NPLOC4/TSPAN10 (17q25.3) gene cluster, which has previously been linked to myopia and other ocular disturbances (e.g., Plotnikov et al., 2019), was also associated with astigmatism (Shah, Li et al., 2018). Another study in individuals from the UK

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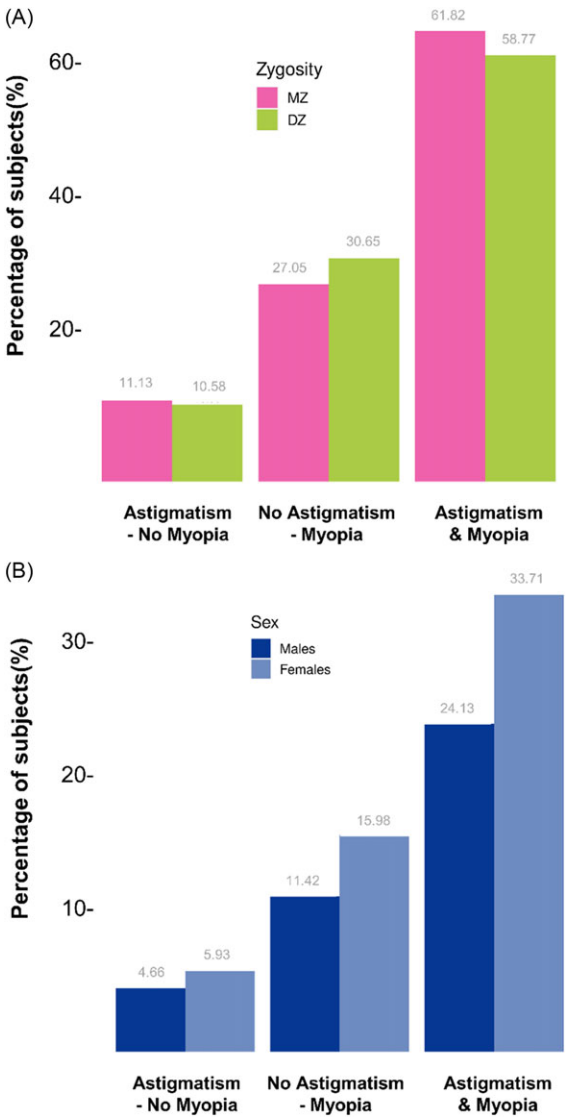

Figure 3. Prevalence of astigmatism, myopia, and their comorbidity in the sample. Three groups are shown: Astigmatism and No myopia; No astigmatism and Myopia; Astigmatism and Myopia. Segregated by zygosity (A) or by sex (B). No differences between groups were observed by zygosity: monozygotic (MZ) vs. dizygotic (DZ), $\chi^2(2, N = 1424) = 2.21$, $p = .33$, nor by sex, $\chi^2(2, N = 1424) = 0.23$, $p = .89$.

and Canada showed that keratoconus, a corneal deformity and thickness associated with early stages of myopia and astigmatism, involved approximately 500 genetic loci, suggesting a highly polygenic architecture of ocular refraction errors (He et al., 2022). The present study highlights the genetic overlap between astigmatism and myopia, and further research is needed to identify the specific shared or unique loci contributing to the etiology of these conditions. The higher concordance rates and heritability estimates in this study indicate that these refractive errors have a strong genetic contribution in the Mexican population.

Our results are consistent with prior research on the heritability of astigmatism and myopia in various populations. For astigmatism, studies have demonstrated higher correlations within MZ twins compared to DZ twins for factors such as refractive error, axial length, and corneal curvature (Dirani et al., 2008; Lyhne et al., 2001; Teikari et al., 1989). In the case of myopia, a Chinese study found a higher concordance rate in MZ twins (.65) than in DZ twins (0.46) (Lin & Chen, 1987). Our findings, with concordance rates of .74 and .55 for MZ and DZ twins respectively reveal a similar trend. Currently, it is understood that myopia results from the interplay of multiple genes and genetic variants that influence eye growth and retinal signaling (Williams et al., 2017).

The demographic analyses showed no differences in the distribution of age nor sex between MZ and DZ twins, suggesting that differences in demographics ($p > .05$) do not explain our results. Additionally, our results show a higher prevalence of myopia (45%) than astigmatism (36%) in the Mexican population, which is consistent with those previously observed by Gomez-Salazar et al. (2017). Additionally, there was a higher number of participants that reported being diagnosed with both astigmatism and myopia, instead of only one diagnosis, and this is not different as a function of zygosity (MZ vs. DZ) or sex (MZ vs. DZ). This finding suggests a phenotypic link between these two traits.

While biometric measures are used to diagnose astigmatism, for example, measuring the meridian of anterior corneal surface (also known as K1) and the steep meridian of the anterior corneal surface (also known as K2) to estimate the spherical equivalent and the autorefraction of the eyes (Dirani et al., 2008), we had no access to any of these values. Requesting such information can limit the extent of participant recruitment, particularly in populations like those in Mexico, where obtaining large sample sizes with these biometric measures is a geographic and economic challenge. In these circumstances, participant self-reported data acquired through online methods can offer a significant advantage for twin studies, particularly in terms of size and geographic representation (Grjibovski et al., 2006; Hur et al., 2019).

Our results were robust even when considering reports for the pair from only one of the twins. The primary analysis conducted on 1399 families and the analysis on 243 complete pairs both replicated the results for myopia and astigmatism. Furthermore, the consistency of participant and co-twin reports was observed to be high, with 80.45% agreement for astigmatism and 84.36% for myopia. This suggests that the participant and co-twin reports were highly reliable and supports the value of using participant-reported data in twins' studies, especially when only one of the twins can provide information. This method allows the effective use of data obtained through electronic records, making research possible for underrepresented populations. Nevertheless, further research should compare the in-person physical examination and participant-reported data to assess the similarity and reliability of results and address this inherent limitation when using participant-reported data.

One shortcoming of the study is that the limited sample size prevented us from conducting subgroup analyses by zygosity and sex. Future research should aim to overcome this limitation by increasing the sample size, in order to investigate genetic differences as a function of sex in greater detail. Although a high reliability (above 85%) between perceived zygosity and DNA-tested zygosity has been reported (J. Chen et al., 2010; Hardiansyah et al., 2021; Ooki & Asaka, 2004; Reed et al., 2005), another inherent limitation in this study is that the DNA validation of the zygosity was not performed; further research might address the concern for this Mexican sample.

Also, given the high genetic influence demonstrated in the current results, it is also desirable to explore possible genetic factors and variations in the Mexican population through techniques such as GWASs (Nakanishi et al., 2009; Shah, Li et al., 2018). In addition to the strong genetic contribution identified here, it is relevant to note that, according to the model fitting, the shared environmental

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Table 1. Astigmatism concordance rates in Mexican twins

Group		Total *n*	Pairs	Positive cases *n*	Negative cases *n*	Concordant pairs	Discordant pairs	Probandwise concordance rate	95% CI
MZ	MZF	1098	549	439	659	165	109	0.75	0.71, 0.79
	MZM	462	231	138	324	49	40	0.71	0.63, 0.79
DZ	DZF	612	306	249	363	74	101	0.59	0.53, 0.66
	DZM	166	83	40	126	11	18	0.55	0.40, 0.70
	DZOS	460	230	150	310	36	78	0.48	0.40, 0.56
	All MZ	1560	780	577	983	214	149	0.74	0.71, 0.78
	All DZ	1238	619	439	799	121	197	0.50	0.50, 0.60
	Total	2798	1399	1016	1782	335	346	0.66	0.63, 0.69

Note: MZ, monozygotic; DZ, dizygotic; MZF, monozygotic female; MZM, monozygotic male; DZF, dizygotic female; DZM, dizygotic male; DZOS, dizygotic opposite sex. Probandwise concordance between All MZ and All DZ groups was tested by Likelihood Ratio Test. $\chi^2(1)= 40.20$, $p = 2.29 \times 10^{-10}$. Significant concordance rate difference between groups was observed.

Table 2. Myopia concordance rates in Mexican twins

Group		Total *n*	Pairs	Positive cases *n*	Negative cases *n*	Concordant pairs	Discordant pairs	Probandwise concordance rate	95% CI
MZ	MZF	1098	549	538	560	209	120	0.69	0.64, 0.74
	MZM	462	231	165	297	65	35	0.47	0.33, 0.61
DZ	DZF	612	306	321	291	111	99	0.58	0.51, 0.65
	DZM	166	83	51	115	12	27	0.78	0.74, 0.81
	DZOS	460	230	194	266	56	82	0.79	0.73, 0.85
	All MZ	1560	780	703	857	274	155	0.74	0.71, 0.78
	All DZ	1238	619	566	672	179	208	0.55	0.50, 0.60
	Total	2798	1399	1269	1529	453	363	0.66	0.63, 0.69

Note: MZ, monozygotic; DZ, dizygotic; MZF, monozygotic female; MZM, monozygotic male; DZF, dizygotic female; DZM, dizygotic male; DZOS, dizygotic opposite sex. Probandwise concordance between All MZ and All DZ groups was tested by Likelihood Ratio Test. $\chi^2(1) = 33.09$, $p = 8.80 \times 10^{-9.}$ Significant concordance rate difference between groups was observed.

Table 3. Astigmatism concordance rate in pairs of Mexican twins

Group	Total *n*	Pairs	Positive cases *n*	Negative cases *n*	Concordant pairs	Discordant pairs	Probandwise concordance rate	95% CI
All MZ	324	162	151	173	55	41	0.73	0.66, 0.80
All DZ	162	81	66	96	15	36	0.45	0.33, 0.57
Total	486	243	217	269	70	77	0.65	0.58, 0.71

Note: MZ, monozygotic; DZ, dizygotic. Probandwise concordance between All MZ and All DZ groups was tested by Likelihood Ratio Test. $\chi^2(1) = 14.72$, $p = 1.20 \times 10^{-4}$. Significant concordance rate difference between groups was observed.

Table 4. Astigmatism concordance rate in pairs of Mexican twins

Group	Total *n*	Pairs	Positive cases *n*	Negative cases *n*	Concordant pairs	Discordant pairs	Probandwise concordance rate	95% CI
All MZ	324	162	178	146	72	34	0.81	0.75, 0.87
All DZ	162	81	77	85	23	31	0.60	0.49, 0.71
Total	486	243	255	231	95	65	0.75	0.69, 0.80

Note: MZ, monozygotic; DZ, dizygotic. Probandwise concordance between All MZ and All DZ groups was tested by Likelihood Ratio Test. $\chi^2(1) = 12.08$, $p = 5.0 \times 10^{-4}$. Significant concordance rate difference between groups was observed.

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Table 5. Model fitting for ACE model and comparison with more parsimonious models

	Model fit -2lnL*	Δ*DF*	AIC	ΔAIC	*p*	Compare with model
ACE	5892.591		5914.59	0		
ADE	5896.232	0	5918.23	3.64		ACE
CE	5944.11	3	5960.23	45.52	<.001	ACE
AE	**5896.467**	**3**	**5912.47**	**−2.12**	**.275**	**ACE**
E	6451.833	6	6461.83	547.24	<.001	ACE

Note: *2 × log likelihood. AIC, Akaike information criterion. The AE model in bold type showed the best fit according to the AIC. Each model is compared to the original ACE; the *p* value shows whether the fitting of the model significantly decreased after removing a parameter, such as A in CE or C in AE models. Consequently, the AE model $p = .275$ did not differ and to favor parsimony this was selected as the best one.

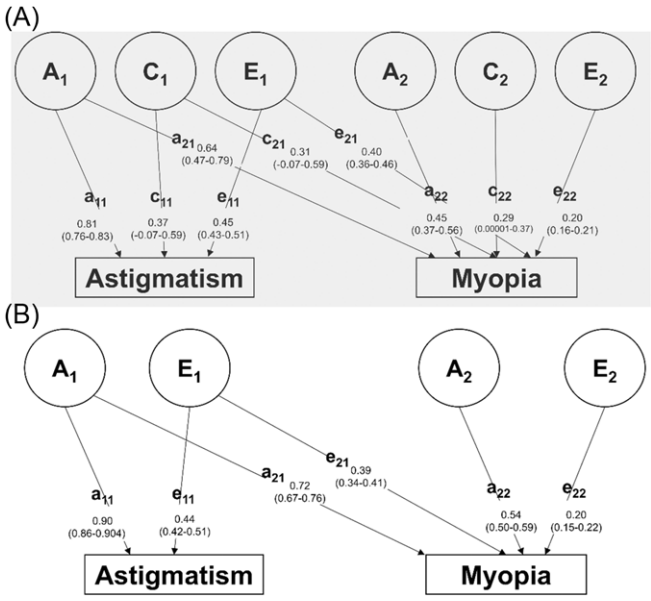

Figure 4. Bivariate path model for astigmatism and myopia. A. Estimates and 95% CI for the full ACE model (fitting: −2 × log likelihood = 5892.59). B. Adjusted estimates and 95% CI for the AE model, which was suggested by the AIC (ΔAIC = −2.12) with the best fitting (−2 × log likelihood = 5896.4) as the most parsimonious model.
Note: ACE model refers to the additive genetic (A) effects, and common (C), and unique (E) environmental influences on a trait. AIC, Aikake information criterion.

influence was not significant enough to be included in the model, suggesting that the common lifestyle in the twins' families has no significant influence on the variability of being diagnosed with astigmatism or myopia. However, it is also important to consider individual environmental factors such as nutrition, the use of electronic devices, and near-work to be explored in future Mexican twin samples to understand their role in the prevalence in different traits, including refractive errors.

Finally, it is not unexpected that one of the first twin studies focused on examining the concordance rates of refraction errors in human eyes. Twin studies afford a unique chance to investigate conditions such as astigmatism and myopia. In conclusion, our study affirms that the likelihood of developing astigmatism and myopia in the Mexican population is significantly shaped by genetic factors.

Data availability statement. The data and analyses supporting the findings of this study will be available after accepted publication at GitHub URL: https://github.com/NeuroGenomicsMX/TwinsMX_Astigmatism_Myopia. Personal data containing information that could compromise the privacy of the participants will not be available.

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Competing interests. None.

Ethical statement. The study protocol was reviewed and approved by the Research Ethics Committee of the Institute of Neurobiology at UNAM. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

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