

The myopic phenotype in children with inherited retinal disease – key insights from a UAE series

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Abstract

Background

To describe the clinical characteristics of childhood myopia in children with genetically confirmed inherited retinal disease (IRD) and to evaluate the frequency with which commonly stated 'red flag' features of secondary myopia were present.

Methods

This retrospective single-centre case series included children (<18 years) with bilateral myopia and genetically confirmed IRD presenting between January 2021 and January 2026. Demographic characteristics, presenting symptoms, best-corrected visual acuity (BCVA), cycloplegic refraction, family history, ocular findings, genotype and longitudinal refractive progression were recorded. The proportions of children with high myopia (≤ -6.00 D) before 10 years of age and myopia exceeding chronological age were determined.

Results

51 children were included, of whom 37 were male (72.5%). The mean age at presentation was 7.4 years and the mean follow-up was 3.9 years. Reduced BCVA was present in all patients at presentation. Nyctalopia and/or photophobia were reported by 46 children (90.2%). A family history of IRD was present in 30 (58.8%), nystagmus in 12 (23.5%), systemic abnormalities in 8 (15.7%) and strabismus in 2 (3.9%). High myopia before 10 years of age was present in 17 (33.3%), while only 15 (29.4%) demonstrated myopia exceeding their chronological age.

Conclusions

Reduced BCVA together with nyctalopia/photophobia were the most common features, whereas the frequently cited screening criteria of high myopia before 10 years of age and myopia exceeding age were present in only a minority of patients. These findings indicate that overreliance on refractive data alone may fail to identify many children with secondary myopia associated with underlying IRD.

Introduction

Childhood myopia has become an increasingly important global public health concern owing to its rising prevalence and associated risk of lifelong ocular morbidity.¹ Although the majority of cases represent primary juvenile-onset myopia, a smaller proportion occur secondary to underlying ocular or systemic disease. Distinguishing secondary from primary myopia is clinically important because children with secondary myopia frequently require additional investigations, multidisciplinary management, genetic counselling and surveillance for associated systemic manifestations.²

IRDs comprise a genetically and phenotypically heterogeneous group of disorders characterised by inherited stationary or progressive retinal dysfunction.³ Childhood myopia is a recognised feature in several forms of IRD, in particular in congenital stationary night blindness, cone and cone-rod dystrophies.⁴ Early diagnosis, however, may be challenging because refractive error can precede characteristic retinal abnormalities, particularly in younger children in whom symptoms may be subtle or difficult to elicit. Delayed recognition may postpone molecular diagnosis, appropriate counselling, screening for associated systemic disease and access to emerging gene-based therapies.⁵ Furthermore, the efficacy and safety of many contemporary myopia-control interventions have not been studied or established in children with secondary myopia associated with IRD.

Due to the importance of early and accurate detection of secondary myopia related to IRD, several clinical features have been proposed as screening criteria, most commonly the development of high myopia before 10 years of age and myopia exceeding the child's chronological age in dioptres.^{6,7} These criteria in particular have been incorporated into numerous clinical guidelines, consensus statements and referral pathways for childhood myopia.^{2,6} However, the frequency with which these features occur in genetically confirmed IRD has not been systematically evaluated. Similarly, the longitudinal pattern of refractive progression in children with IRD remains incompletely characterised, with the existing literature largely limited to small disease-specific series.⁴

This study describes the clinical phenotype of childhood myopia in a cohort of children with genetically confirmed IRD at a tertiary referral centre in the United Arab Emirates and specifically characterises the frequency of the above-mentioned screening criteria. We also describe the rate of myopic progression within this cohort.

Methods

This retrospective observational case series was conducted at a tertiary referral hospital in the United Arab Emirates. Institutional Research Ethics Board approval was obtained before study commencement, and the study adhered to the tenets of the Declaration of Helsinki. The requirement for informed consent was waived because of the retrospective study design.

Electronic medical records of consecutive children presenting between January 2021 and January 2026 were reviewed. Eligible patients were younger than 18 years at presentation, had bilateral myopia (cycloplegic spherical equivalent [SER] ≤ -0.50 D) and a molecularly confirmed diagnosis of IRD. Patients without genetic confirmation, those presenting after 18 years of age or those with incomplete clinical records were excluded.

Demographic characteristics, including age at presentation, sex, ethnicity and family history of IRD, were recorded. Presenting symptoms of nyctalopia and/or photophobia, together with the presence of nystagmus, strabismus and associated systemic abnormalities, were extracted from the clinical record. Best-corrected visual acuity was recorded using age-appropriate visual acuity testing. Cycloplegic

refraction was performed following administration of two drops of 0.5% cyclopentolate separated by 30 minutes. SER was calculated at presentation and subsequent follow-up visits. Annual refractive progression was calculated as the change in SER between the initial and final cycloplegic refractions divided by the duration of follow-up in years. Observed mean annual progression rates were compared with published age-matched normative data for myopic children reported by Bullimore and colleagues.⁸

All patients underwent comprehensive ophthalmic examination. Where clinically feasible, multimodal retinal imaging included ultra-widefield colour fundus imaging and fundus autofluorescence (Optos plc, Dunfermline, UK) together with spectral-domain optical coherence tomography (Heidelberg Spectralis OCT; Heidelberg Engineering GmbH, Heidelberg, Germany). Patients with clinical findings suggestive of inherited retinal disease underwent electrodiagnostic testing, most commonly full-field electroretinography (Diagnosys Espion; Diagnosys LLC, Lowell, MA, USA), followed by molecular genetic testing. Genetic diagnoses were established using whole-genome sequencing performed through accredited diagnostic laboratories participating in the Emirati Genome Programme.

Continuous variables are presented as mean $\pm$ 95% confidence intervals (CI) and categorical variables as frequency/percentage and CI. Mean annual refractive progression was compared with published age-matched normative progression using a two-sided one-sample *t*-test.⁸ Statistical analyses were performed using IBM SPSS Statistics version 31.0 (IBM Corp., Armonk, NY, USA), with statistical significance defined as $P < 0.05$.

Results

A total of 51 Emirati children with bilateral myopia and genetically confirmed IRD met the study inclusion criteria. 37 patients (72.5%) were male. The mean age at presentation was 7.4 ± 3.8 years, and the mean duration of follow-up was 3.9 ± 3.5 years. A positive family history of IRD was present in 29 patients (56.9%), while 8 children (15.7%) had associated systemic abnormalities. Nystagmus was identified in 12 patients (23.5%) and strabismus in 2 (3.9%). Baseline demographic and clinical characteristics are summarised in Table 1. Reduced best-corrected visual acuity (BCVA) was present in every patient at presentation, with BCVA ranging from 0.10 LogMAR (20/25) to 1.90 LogMAR (counting fingers). No child achieved a BCVA of 0.00 LogMAR (20/20) or better in either eye.

Symptoms of retinal dysfunction were common at presentation. Nyctalopia and/or photophobia were reported by 46 children (90.2%), making these the most frequently documented presenting symptoms. Therefore, reduced BCVA together with symptoms of retinal dysfunction represented the predominant clinical phenotype within this genetically confirmed cohort. A positive family history of IRD was present in over half of patients (58.8%), whereas nystagmus, systemic abnormalities and strabismus were considerably less frequent. The frequency of individual clinical features is summarised in Table 2.

Whole-genome sequencing identified pathogenic variants across a broad spectrum of inherited retinal disease genes. *KCNV2* was the most frequently identified genotype, accounting for 22 of 51 patients

(43.1%). Other pathogenic variants included *MERTK* (9.8%), *TRPM1* (7.8%), *RPGR* (7.8%), *ABCA4* (5.9%), *MFSD8* (5.9%), *IMPG2* (5.9%), *TULP1* (3.9%), *INPP5E* (3.9%), *RGS9* (3.9%) and *CLDN19* (2.0%). The distribution of molecular diagnoses is presented in Table 3.

The magnitude of myopia at presentation varied substantially across the cohort. Despite this variability, only 15 children (29%) demonstrated myopia exceeding their chronological age at any stage during follow-up. Similarly, only 17 children (33%) developed high myopia ($\text{SER} \leq -6.00$ D) before 10 years of age. These findings indicate that the refractive characteristics commonly proposed to screen for secondary myopia were present in only a minority of children with genetically confirmed IRD.

Serial cycloplegic refractions were available for 32 of the 51 children (63%), with a mean follow-up duration of 3.9 years. Mean annual refractive progression was -0.41 ± 0.11 D/year. Compared with published age-matched data in primary myopes reported by Bullimore and colleagues, annual refractive progression within the study cohort was numerically lower but did not reach statistical significance ($P = 0.09$).⁷ Similarly, among children who developed high myopia before 10 years of age, the annual rate of progression also tended to be lower than published normative myopic progression values, although this difference also did not reach statistical significance ($P = 0.19$).⁷ Therefore overall, although several children presented with moderate or high myopia at an early age, subsequent refractive progression was generally modest during the follow-up period.

Discussion

Childhood myopia is a recognised feature in a wide range of IRDs; however, differentiating secondary from primary juvenile-onset myopia has become increasingly challenging.⁴ This is in part due to the prevalence of childhood myopia continuing to rise, with onset occurring at earlier ages, leading to higher magnitudes of myopia. In this retrospective series of patients with genetically confirmed IRD and myopia, reduced BCVA was present in every patient at presentation. In addition, symptoms of retinal dysfunction, particularly nyctalopia and photophobia, were reported by 90% of children or their parents. In contrast, the commonly cited criteria used to prompt further investigation of possible secondary myopia, including high myopia before 10 years of age and myopia exceeding chronological age, were present in only approximately one-third of patients.^{2,6} These findings suggest that reliance on refractive error alone, whether in referral criteria or clinic protocols, may fail to identify a substantial proportion of children with underlying inherited retinal disease.

Previous reports have established an association between childhood myopia and several IRDs, including congenital stationary night blindness and cone and cone-rod dystrophies. However, relatively few studies have examined the clinical presentation of these children from the perspective of a paediatric myopia service.⁸ In particular, refractive status alone is highly variable in several disorders represented within our cohort, including *KCNV2*-associated cone dystrophy with supernormal rod response, where affected individuals may be myopic, emmetropic or hyperopic. In light of this, some of the patients in our cohort may have had typical juvenile-onset myopia with a non-causative coexisting IRD and thus not true

‘secondary myopia’. However, even in these cases, the identification of the underlying IRD is still important in the myopia management strategy due to the lack of evidence of the efficacy and safety of current myopia-control interventions in this population. Therefore, maintaining a heightened suspicion in patients who have reduced BCVA or the other features identified is still important for the detection of causative or coexisting IRD in the context of myopia.

Our findings extend the existing literature by demonstrating that nyctalopia/photophobia symptoms and reduced BCVA were considerably more frequent than the refractive screening criteria commonly referred to in the literature for detecting secondary myopia. Although our observations should not be interpreted as measures of diagnostic performance in the absence of a comparison cohort, they highlight the importance of careful history taking and accurate assessment of best-corrected visual acuity when evaluating children with myopia.

A secondary finding of this study was that annual refractive progression tended to be lower than published age-matched normative data, although the difference did not reach statistical significance. Similar findings were observed among children with early-onset high myopia. These observations suggest that, once established, refractive progression in children with IRD may not necessarily differ substantially from that observed in primary juvenile-onset myopia, or may in fact be slower. However, these comparisons should be interpreted cautiously because they were performed against historical normative data from European children rather than a contemporaneous ethnically matched control cohort.⁷

Our findings have practical implications for clinicians involved in paediatric myopia management. Myopia management is increasingly protocol-driven, with decisions to refer patients from the community to hospital eye services or to initiate further investigations in clinic often based predominantly on refractive characteristics.^{2,6} Our results suggest that these criteria alone may fail to identify a large proportion of children with coexisting IRD. Assessment of visual acuity, symptoms of retinal dysfunction and family history therefore remain integral components of the clinical evaluation of children presenting with myopia. Furthermore, the evidence supporting atropine, orthokeratology, multifocal contact lenses, peripheral defocus spectacle lenses and repeated low-level red-light therapy has been generated almost exclusively in children with primary myopia.⁹⁻¹⁹ The effectiveness and safety of these interventions in IRDs remain uncertain; therefore, accurate early diagnosis of children with secondary myopia is important prior to routine implementation of myopia-control interventions.^{20,21}

This study has several strengths, including molecular confirmation of all diagnoses, comprehensive retinal phenotyping and one of the largest reported paediatric cohorts examining myopia associated with IRD from the Gulf region.

Several limitations should also be acknowledged. First, the retrospective design introduces the potential for selection and documentation bias. Second, the cohort was derived from a tertiary referral centre and may therefore overrepresent more severe phenotypes. We did not include a contemporaneous

comparison group of children with primary myopia; consequently, the study describes the frequency of clinical features within an IRD cohort but is not intended to determine their diagnostic specificity or predictive value. Fourth, comparisons of refractive progression were made using published normative data from European children rather than an ethnically matched control population. Finally, progression analyses were based on serial cycloplegic spherical equivalent refraction rather than axial length measurements, which were not consistently available.

Future prospective comparative studies including children with both primary and secondary myopia are required to determine the diagnostic accuracy of these clinical features and to evaluate the safety and effectiveness of contemporary myopia-control interventions in inherited retinal disease.

Conclusion

In this genetically confirmed cohort of children with myopia and associated IRD, reduced BCVA and symptoms of retinal dysfunction were the most common presenting features, whereas high myopia before 10 years of age and myopia exceeding chronological age were observed in only a minority of patients. These findings suggest that overreliance on refractive criteria when determining who to investigate further for possible secondary myopia may miss many children with underlying IRD. Prospective comparative studies are required to establish the diagnostic performance of these clinical features and to inform evidence-based management strategies as molecular therapies and myopia-control interventions continue to evolve.

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Tables

Table 1. Baseline demographic and clinical characteristics (n=51)

Variable	Value (95% CI)
Number of patients	51
Male sex	37 (72.5%)
Mean age at presentation (years)	7.4 (6.4–8.4)
Mean age at final follow-up (years)	11.0 (9.8–12.1)
Mean follow-up (years)	3.9 (2.8–5.0)
Mean BCVA RE (logMAR)	0.74 (0.64–0.84)
Mean BCVA LE (logMAR)	0.75 (0.65–0.85)

Table 2. Clinical indicators for identifying inherited retinal dystrophy in myopic children (n=51)

Clinical feature	Number	Percentage (95% CI)
Best-corrected visual acuity <20/20	51	100 (93.2-100)
Nyctalopia and/or photophobia	46	90.2 (77.2-94.6)
Positive family history	29	56.9 (44.3-70.0)
Nystagmus	12	23.5 (13.8-36.0)
Systemic abnormalities	8	15.6 (8.1-27.4)
Strabismus	2	3.9 (1.1-12.8)
High myopia (≤ -6.00 D) before 10 years	17	33.3 (21.6-46.1)
Myopia greater than chronological age	14	27.4 (18.4-42.1)

Table 3. Distribution of pathogenic genetic variants

Gene	n (%)
KCNV2	22 (43.1%)
MERTK	5 (9.8%)
TRPM1	4 (7.8%)
RPGR	4 (7.8%)
ABCA4	3 (5.9%)
MFSD8	3 (5.9%)
IMPG2	3 (5.9%)
TULP1	2 (3.9%)
INPP5E	2 (3.9%)
RGS9	2 (3.9%)
CLDN19	1 (2.0%)