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Evaluation of Treatment Response in Pediatric Iron Deficiency and Mixed Anemias Using Optical Coherence Tomography: A Prospective Study

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Abstract

Objective

The aim of this study was to investigate the effects of iron deficiency anemia and mixed type anemia (iron deficiency + vitamin B12 deficiency) on hematological/biochemical profiles and retinal parameters obtained from optical coherence tomography measurements in children aged 4–18 years, and to compare structural changes before treatment and one month after treatment.

Materials and Methods

This prospective and observational study was conducted at Van Yüzüncü Yıl University between April 1, 2024, and March 1, 2025. A total of 80 children were included in the study: 35 with iron deficiency anemia (IDA), 19 with mixed anemia, and 26 healthy controls. Clinical-demographic data, hematological, biochemical, and inflammatory parameters were recorded; bilateral RNFL (Retinal Nerve Fiber Layer) quadrants, mean RNFL, macular, and choroidal thicknesses were measured using OCT. Measurements were analyzed using a blinded method. The IDA group received oral Fe^{3+}, while the mixed anemia group received intramuscular hydroxocobalamin treatment in addition to the same iron treatment; laboratory and OCT measurements were repeated after 4 weeks. Statistical analyses were performed using SPSS software, and a significance level of $p < 0.05$ was accepted.

Results

Significant differences were found between the groups in terms of age and gender distribution. When the three groups were compared, significant differences were observed in hemoglobin, hematocrit, erythrocyte indices, RDW, and iron metabolism indicators. In the IDA group, post-treatment RBC, hemoglobin, hematocrit, MCV, MCHC, serum iron, ferritin, and transferrin saturation increased; total iron binding capacity decreased, and RDW decreased. In the mixed anemia group, post-treatment hemoglobin and hematocrit values increased significantly; vitamin B12, folate, and iron stores improved, and inflammatory markers remained stable. In OCT evaluation, in the mixed group, only subfoveal choroid thickness was significantly increased in the right eye; in the IDA group, nasal, inferior, and global RNFL values decreased, and choroid thickness increased in the right eye. In the mixed group, no significant changes were found in left eye OCT parameters; in the IDA group, significant changes were observed in nasal and inferior RNFL and choroid thickness in the left eye.

Conclusion

The findings indicate that iron replacement and, in mixed cases, iron and hydroxocobalamin therapy lead to hematological improvement; some ocular microstructural parameters monitored by OCT may change

with treatment response. These data suggest that OCT may have potential contribution to monitoring in the multidisciplinary evaluation of pediatric anemia. Studies with longer follow-up periods and larger sample sizes are needed.

1. Introduction

Iron deficiency anemia (IDA) and mixed anemia (iron deficiency + vitamin B12 deficiency), where both deficiencies occur together, are among the common hematological problems in childhood and adolescence. These conditions reduce the oxygen-carrying capacity of hemoglobin, leading to negative effects on growth, development, and overall health (1). Iron deficiency, especially in childhood, manifests with symptoms such as weakness, fatigue, and paleness; while vitamin B12 deficiency can cause neurological and ophthalmological complications in addition to hematological findings (2).

Eye tissues are sensitive to systemic nutrient deficiencies due to their high metabolic requirements. Iron and vitamin B12 deficiencies can lead to microscopic structural changes in structures such as the retina and optic nerve; these changes can manifest clinically as blurred vision, color perception disorders, and optic disc pallor (3). OCT is an imaging method that allows for non-invasive and high-resolution evaluation of the retina and optic nerve fiber layer, objectively revealing microscopic structural changes (4).

Studies on structural changes detected by OCT in children with iron and vitamin B12 deficiency are limited in the literature, and data comparing pre-treatment and short-term post-treatment changes are insufficient. Therefore, revealing the effects of hematological deficiencies on eye tissues and objectively evaluating the response to treatment is of clinical importance.

The aim of this study is to evaluate the findings of the retina, optic nerve, and retinal nerve fiber layer using OCT in children aged 4–18 years diagnosed with iron deficiency anemia and mixed type anemia, and to compare structural changes before treatment and 1 month after treatment. In addition, it is aimed to reveal the potential contribution of OCT in the follow-up of this patient group. In this study, it is hypothesized that measurable changes in retinal nerve fiber layer and choroid thickness may occur in children with iron deficiency anemia and mixed type anemia in parallel with hematological improvement after treatment.

2. Materials and Methods

2.1. Study Design

This study was designed as prospective and observational. It aimed to evaluate microscopic structural changes in the eye using optical coherence tomography (OCT) in children diagnosed with iron deficiency anemia and mixed (iron + B12) anemia. Patients were examined for retina, optic nerve, and RNFL using OCT before treatment and 1 month after treatment.

The study was conducted at the General Pediatric Polyclinic of the Department of Pediatrics, Faculty of Medicine, Van Yüzüncü Yıl University between April 1, 2024, and March 1, 2025. Children aged 4–18 years without known chronic diseases were included in the study. A total of three groups were evaluated in the study: 35 patients with iron deficiency anemia, 19 patients with mixed anemia, and 26 healthy controls.

2.1.1. Clinical and Demographic Assessment

The age and gender information of all participants, as well as their hematological parameters (RBC, hemoglobin, hematocrit, MCV, MCHC, WBC, platelets), inflammatory markers (CRP, sedimentation), iron metabolism indicators (serum iron, ferritin, total iron binding capacity, transferrin saturation), LDH, vitamin B12 and folate levels were recorded. In the ophthalmological assessment, bilateral RNFL thickness, macular thickness and choroidal structures were measured with OCT; the temporal, superior, inferior and nasal quadrants of the RNFL and their mean values were analyzed.

2.1.2. Data Collection Process

Laboratory and ophthalmological data were obtained from examinations performed at Van Yüzüncü Yıl University Faculty of Medicine Hospital, recorded in the SPSS program, and analyzed.

2.1.3. Participant Selection Criteria

Children aged 4–18 years were included in the study. The iron deficiency anemia group consisted of cases with hemoglobin levels below the anemia threshold for their age and serum ferritin levels < 12 ng/mL. The mixed anemia group consisted of cases with hemoglobin levels below the anemia threshold for their age, serum ferritin levels < 12 ng/mL, and serum vitamin B12 levels < 200 pg/mL. The control group consisted of healthy individuals with hemoglobin and hematocrit values within the normal limits for their age, and ferritin and vitamin B12 levels within the normal range. Individuals with thalassemia, sickle cell anemia, leukemia, or other chronic systemic diseases, as well as those with cataracts, optic disc anomalies, or chronic eye diseases that could affect OCT measurements, were excluded from the study.

2.1.4. Ophthalmological Evaluation and Treatment Protocol

OCT measurements were performed at the Department of Ophthalmology, Dursun Odabaş Medical Center, Van Yüzüncü Yıl University, using a Heidelberg Engineering Spectralis OCT device. Measurements were analyzed using a blinded method where evaluators were unaware of the patient groups. Patients with iron deficiency anemia received oral Fe^{3+} therapy (4–6 mg/kg/day loading dose, followed by 2–3 mg/kg/day maintenance dose). Patients with vitamin B12 deficiency in the mixed anemia group received standard intramuscular hydroxocobalamin therapy in addition to the same iron therapy. Hydroxocobalamin therapy was administered daily for the first week, twice a week for the second week, and once a week for the third and fourth weeks. All patients were monitored for 4 weeks, and laboratory and OCT measurements were repeated after treatment.

2.2. Ethics Committee Approval

The study was approved by the Van Yüzüncü Yıl University Faculty of Medicine Clinical Research Ethics Committee with decision number 03 dated 27.03.2024. It was conducted in accordance with the principles of the Helsinki Declaration, and written consent was obtained from the families of all participants.

2.3. Limitations of the Study

The study's single-center nature and relatively small number of patients limit the generalizability of the results. Furthermore, although initially planned to evaluate iron deficiency, pure vitamin B12 deficiency, and mixed anemia groups separately, the insufficient number of cases with pure vitamin B12 deficiency resulted in analyses being conducted only on the iron deficiency anemia and mixed anemia groups. The limited follow-up period of 4 weeks may also have made it difficult to assess longer-term changes in neuro-ophthalmological effects, particularly those related to vitamin B12 deficiency.

2.4. Sample Size

The primary endpoint of the study was defined as retinal nerve fiber layer (RNFL) thickness. A one-way analysis of variance (ANOVA) power analysis was performed for three independent groups (iron deficiency anemia, mixed anemia, and healthy control). Based on the standard deviation reported in the literature for the same age group (39.8 μm) and the clinically significant group difference (30.5 μm), Cohen's effect size f was calculated as 0.54. At $\alpha = 0.05$ and 80% power, a minimum of 12 participants per group was deemed sufficient. Considering a possible 10% loss, the target sample size was planned as 14 cases per group. The current sample size, including 35 iron deficiency anemia, 19 mixed anemia, and 26 control cases, exceeded the calculated minimum value.

2.5. Statistical Analysis

Statistical analyses were performed using SPSS Windows 27.0 (SPSS Inc., Chicago, IL, USA) software. Continuous variables were presented as mean ± standard deviation or median (interquartile range) according to their distribution characteristics, while categorical variables were presented as number and percentage. Normality was assessed using the Shapiro–Wilk test, and homogeneity of variance was assessed using the Levene test. For intergroup comparisons, one-way analysis of variance (ANOVA) or the Kruskal–Wallis test was used as appropriate. In cases where significance was found, post-hoc analysis was applied using the Bonferroni test when homogeneity of variance was achieved, and the Games–Howell test when it was not; for non-parametric comparisons, the Mann–Whitney U test was applied. For pre- and post-treatment within-group comparisons, the dependent samples t-test was used for variables showing normal distribution, and the Wilcoxon signed-rank test was used for variables not showing normal distribution. The statistical significance level was accepted as $p < 0.05$.

3. Findings

3.1. Patient Population

The study included 35 patients with iron deficiency anemia, 19 patients with mixed anemia (both iron and vitamin B12 deficiency), and 26 healthy individuals who met the inclusion criteria. As a result, statistical analysis was performed with a total of 80 participants.

3.2. Basic Descriptive Characteristics

In this study, three groups were compared: patients with iron deficiency anemia, patients with mixed type anemia, and a healthy control group. The mean age of the 26 healthy individuals in the control group was 10.3 ± 3.94 years, with 58% of participants being male (n = 15) and 42% female (n = 11). Hematological and ophthalmological parameters of the control group were found to be within physiological limits, and these data were used as reference values for comparisons with patient groups (Table 1).

Table 1
Baseline demographic, hematological, and OCT characteristics of the control group

Parameter	Value	Unit
Age	10.3 ± 3.94	years
Male/Female	15 / 11	n
Hemoglobin	13.9 (12.8–14.6)	g/dL
MCV	79.6 (77.3–84.6)	fL
Ferritin	29 (23–54)	ng/mL
Global RNFL (right eye)	108 (99–114)	µm
Central macula (left eye)	260 (250–272)	µm
Subfoveal choroid (right eye)	262 (206–308)	µm
Data are presented as mean ± SD or median (IQR).		

The mean age of the 35 patients in the iron deficiency anemia group was 13.5 ± 2.75 years, with 26% of participants being male and 74% female. The median RBC values before treatment were 4.8×10⁶/µL (4.2–5.2), while after treatment they were measured as 5.2×10⁶/µL (4.9–5.6). Hemoglobin levels increased from 9 g/dL (7.4–10.6) before treatment to 12.3 g/dL (10.3–12.9) after treatment. Hematocrit values were 31% (25.6–34.5) before treatment and 38.8% (34.9–42.0) after treatment. Mean erythrocyte volume (MCV) increased from 68 fL (60–73) to 75 fL (68–79), and partial improvement in microcytosis was observed. MCHC values increased from 29.2 g/dL (27.1–30.5) to 31.1 g/dL (29–31.8). Transferrin saturation increased from 5% (4–9) to 15% (9–34), serum iron rose from 20 µg/dL (18–32) to 54 µg/dL (32–88), and total iron stores decreased from 407 µg/dL (354–454) to 325 µg/dL (244–390). Although

ferritin levels increased from 4.3 ng/mL (2.1–5.9) to 14 ng/mL (7–23), complete recovery in iron stores may not have been achieved in all cases (Table 2).

Table 2
Hematological parameters before and after iron therapy in children with iron deficiency anemia (n = 35)

Parameter	Before treatment	After treatment	p-value
Hemoglobin (g/dL)	9 (7.4–10.6)	12.3 (10.3–12.9)	< 0.001
Ferritin (ng/mL)	4.3 (2.1–5.9)	14 (7–23)	< 0.001
MCV (fL)	68 (60–73)	75 (68–79)	< 0.001
Paired comparisons were performed using paired t-test or Wilcoxon signed-rank test.			

The median age of the 19 patients in the mixed type anemia group was 14 years (13–16), with 16% male (n = 3) and 84% female. Post-treatment hemoglobin and MCV levels showed significant improvement; ferritin, vitamin B12, and folate levels increased. Inflammatory markers remained stable throughout the treatment period (Table 4).

Table 4
Hematological and OCT changes before and after combined iron and vitamin B12 therapy in children with mixed anemia (n = 19)

Parameter	Before treatment	After treatment	p-value
Hemoglobin (g/dL)	11.5 (10.2–12.0)	12.9 (12.4–13.4)	< 0.001
Vitamin B12 (pg/mL)	144 (132–166)	329 (234–654)	< 0.005
Subfoveal choroid (μm)	291 (254–314)	321 (281–348)	< 0.05
Combined therapy included oral iron and intramuscular hydroxocobalamin.			

3.3. Comparison Between Groups

3.3.1. Comparison of Three Groups

When the groups were compared, it was found that the mean age of the control group was significantly lower than that of the patient groups (p = 0.001) and the proportion of male individuals was higher (p = 0.005). Kruskal-Wallis analysis revealed that hemoglobin, hematocrit, MCV, MCHC, RDW, ferritin, serum iron, transferrin saturation, and TDBK parameters showed significant differences between the three groups (p < 0.001). RDW values were increased in both anemic groups compared to the control group. CRP and sedimentation values were slightly higher in the patient groups, but did not show a clinically significant increase. No significant differences were found between the groups in terms of ALT, AST, WBC, and neutrophil parameters.

3.3.2. Treatment Response in the Iron Deficiency Anemia Group

After iron replacement, hemoglobin and hematocrit levels increased significantly ($p < 0.001$), and most patients met the criteria for complete hematological response. While a significant increase in ferritin and serum iron levels was observed ($p < 0.001$), total iron deficiency anemia decreased significantly ($p < 0.001$). RDW values decreased significantly ($p < 0.001$), while MCV remained within the normocytic range. No significant changes were observed in CRP and sedimentation values. A statistically significant but clinically insignificant decrease was detected in ALT levels ($p = 0.045$) (Table 2).

3.3.3. Treatment Response in the Mixed Anemia Group

In the mixed anemia group, hemoglobin and hematocrit values increased significantly after iron and hydroxocobalamin treatment ($p < 0.001$), and the hemoglobin level reached an average of 13 g/dL. Vitamin B12 levels increased from an average of 144 pg/mL to 329 pg/mL ($p \leq 0.005$), reaching a sufficient level in terms of the risk of neuro-ophthalmological complications. Significant increases were also observed in ferritin, serum iron, and folate levels. No significant changes were detected in LDH, ALT, and AST values (Table 4).

3.4. Comparison of Post-Treatment and Inter-Group OCT Parameters

In the mixed type anemia group, only subfoveal choroid thickness showed a statistically significant increase in right eye OCT measurements after treatment ($p < 0.05$) (Table 4). In the iron deficiency anemia group, significant changes were observed in the nasal quadrant, inferior quadrant, global RNFL, and choroidal thickness values of the right eye ($p < 0.05$). While nasal, inferior, and global RNFL values decreased after treatment, choroidal thickness increased (Table 3). In the mixed type anemia group, no significant changes were observed in the left eye OCT parameters. However, in the iron deficiency anemia group, significant changes were observed in the nasal quadrant, inferior quadrant, and choroidal thickness of the left eye (Table 3).

Table 3
OCT parameter changes before and after iron therapy in children with iron deficiency anemia

OCT parameter	Before treatment	After treatment	p-value
Global RNFL (μm)	103 (92–110)	98 (90–106)	0.018
Subfoveal choroid (μm)	270.4 ± 46.3	288.9 ± 54.7	0.004
RNFL: retinal nerve fiber layer; OCT: optical coherence tomography.			

4. Discussion

This study investigated the hematological/biochemical profile of iron deficiency anemia and mixed type anemia in children aged 4–18 years and their effects on retinal parameters assessed by OCT. Considering the critical roles of iron and vitamin B12 in growth, neurodevelopment, and hematopoiesis (5, 6), childhood anemia is known to have multifaceted effects that can affect cognitive functions, school performance, behavioral development, and visual system functions, not just hematological conditions (7). In this context, the reflection of systemic hematological changes on ocular structures was evaluated through macula, choroid, and RNFL measurements by OCT; post-treatment changes were statistically analyzed.

4.1. Demographic characteristics and fundamental differences between groups

In our study, significant differences were found in the age and gender distributions of the control, iron deficiency, and mixed type anemia groups. The lower average age and higher male ratio in the control group ($p = 0.001$; $p = 0.005$) may be related to the sampling process and clinical presentation characteristics, or it may be explained by the fact that iron deficiency anemia is more common in girls, especially during adolescence (1, 8). Indeed, the shift of age to older ages in patient groups is associated with the increased prevalence of anemia during adolescence (25). In addition, the clinical findings of anemia becoming more pronounced over time and delays in the timing of symptom detection/presentation may contribute to the formation of age differences (9).

4.2. Interpretation of Hematological and Biochemical Profile

Our findings showed that numerous hematological and biochemical parameters differed significantly in the iron deficiency and mixed type anemia groups. In the mixed type anemia group, Hb, Hct, serum iron, ferritin, transferrin saturation, and MCV values were higher than in the iron deficiency group; however, the higher total blood count (TDBK) in the iron deficiency group ($p < 0.05$) suggests that hematopoiesis is impaired in both groups, but that there is a more “complex” hematological mechanism in mixed type anemia (10). The higher MCV/MCHC in the mixed group is consistent with the megaloblastic component due to B12 deficiency disrupting DNA synthesis, slowing erythropoiesis, and the release of larger volume erythrocytes into circulation (11). In contrast, iron deficiency is characterized by microcytic-hypochromic erythrocytes; Therefore, deviations in the indices in combination deficiency reflect the combined effect of these two mechanisms (12). The higher ferritin level found in the mixed group suggests that iron deficiency may be relatively less dominant in this group, or that the iron stores may not have been completely depleted before treatment (13). Although this study initially planned to evaluate cases of iron deficiency, pure vitamin B12 deficiency, and co-occurring iron deficiency and vitamin B12 deficiency in separate groups, due to the insufficient number of cases with pure vitamin B12 deficiency, the analyses were carried out through iron deficiency and mixed type anemia groups. This situation limited the evaluation of the ocular effects of vitamin B12 deficiency in isolation, but allowed the evaluation of combination anemias, which are more frequently encountered in clinical practice. In addition, the limited

pediatric OCT data on pure B12 deficiency in the current literature supports the interpretability of this approach (16, 21).

4.3. Discussion of Treatment Response

Post-treatment evaluation showed a significant improvement in hematological response in both patient groups (Table 2 and Table 4). In the iron deficiency group, increases in RBC, Hb, Htc, MCV, MCHC, serum iron, ferritin, and transferrin saturation levels, and a decrease in total hematological response (TDR), support the effectiveness of oral iron therapy and appear to be in line with the pediatric literature (14, 15). In the mixed type anemia group, the significant increase in Hb, vitamin B12, folate, and MCHC values demonstrated the contribution of combined treatment to hematological improvement (Table 4). However, the fact that the improvement in some parameters was more limited compared to the iron deficiency group can be explained by the fact that the megaloblastic component may take longer to improve and hematological responses may appear later. In addition, the emphasis on the possibility of more effective intramuscular administration in the treatment of B12 deficiency can also be evaluated within this framework (16). In general, the literature indicates that treatment may be longer and recovery may be slower in combination anemias (8, 17).

4.4. Interpretation of OCT findings: RNFL, choroid and macula

In the iron deficiency anemia group, a significant decrease in RNFL thickness was detected after treatment, especially in the nasal and inferior quadrants and in the G parameter representing the mean RNFL (Table 3). This finding can be explained by the improvement of systemic oxygenation with treatment, the stabilization of the retinal microvascular environment, and the regression of compensatory thickenings secondary to chronic hypoxia. In the literature, it has been reported that such changes in RNFL thickness are more pronounced in the inferior and nasal quadrants in individuals with iron deficiency anemia; it has been suggested that these quadrants may be more sensitive to hypoxia (18–20). The absence of significant changes in RNFL parameters in the mixed type anemia group during a short follow-up period may be related to the slower recovery of megaloblastic effects due to B12 deficiency and processes on myelin synthesis (18, 21). The choroid layer is the ocular structure with the highest vascular density and is directly affected by systemic hematological status (22). In our study, the increase in choroidal thickness after treatment in both patient groups (Tables 3–4) is consistent with the normalization of choroidal circulation and increased microvascular perfusion after the elimination of hypoxia. Data reporting an increase in subfoveal/nasal/temporal choroidal thickness after treatment of iron deficiency anemia support the findings of our study (23). Similarly, there are studies reporting that subfoveal choroidal thickness can be found to be higher in children and adolescents with B12 deficiency (21).

No statistically significant change was detected in macular thickness before and after treatment in either patient group (Tables 3–4). This can be explained by the fact that the macula is an anatomically more stable structure and is more resistant to the early effects of anemia due to its circulation being largely

choroidal in origin. Previous studies in which no significant changes in macular thickness were detected in children with iron deficiency anemia and vitamin B12 deficiency also support this finding (21, 23).

4.5. Bilateral course and interocular parallelism

The observation of similar directional changes in some RNFL and choroid parameters in the right and left eyes in the iron deficiency anemia group suggests that the systemic effect of anemia may be reflected in bilateral ocular structures. In contrast, the more limited and asymmetrical changes in the mixed type anemia group may be related to the short follow-up period and small sample size. It has been previously reported that anemia, a systemic disorder, can cause bilateral effects in the eye (24). However, the more pronounced left eye choroid increase in the iron deficiency group suggests that further studies are needed in terms of individual variations and the dominant eye/perfusion relationship (23).

4.6. Strengths and Limitations

The study's strengths include its multidisciplinary approach, which evaluates hematological parameters and OCT findings together, and its comparative prospective design before and after treatment. However, significant limitations include the relatively limited number of cases, the fact that the study was conducted at a single center, and the inability to separately evaluate the initially planned pure vitamin B12 deficiency group due to insufficient sample size. Furthermore, the short follow-up period may have made it difficult to determine the longer-term implications of neuro-ophthalmological effects, particularly those related to vitamin B12 deficiency.

5. Conclusion

This study has shown that measurable changes in some ocular structural microparameters occur along with hematological improvement in children with iron deficiency anemia and mixed type anemia. After iron replacement and combined treatment in mixed cases, significant improvement in hemoglobin levels and indicators of iron metabolism was achieved in both patient groups; inflammatory and hepatobiliary parameters remained stable.

In OCT evaluations, a decrease was observed in the nasal and inferior RNFL quadrants and mean RNFL thickness, especially in the iron deficiency anemia group after treatment, while a significant increase in choroid thickness was detected. In the mixed type anemia group, no significant changes were observed in RNFL parameters in the short-term follow-up; however, a significant increase in subfoveal choroid thickness was detected. The fact that macular thickness did not change before and after treatment in both groups suggests that the macula may be only minimally affected by anemia in the early stages. The findings reveal that systemic hematological improvement in pediatric anemias may have implications for ocular microvascular structure and RNFL. In this context, OCT can offer clinically valuable information as a complementary, non-invasive method in the evaluation of iron and vitamin B12 deficiency anemias in childhood and in monitoring treatment response. Multicenter studies with longer follow-up periods and larger sample sizes, especially those evaluating pure vitamin B12 deficiency as a separate group, will more clearly reveal the course and clinical significance of the ocular effects of anemia over time. These

findings show that in iron deficiency and mixed type anemias in childhood, not only hematological improvement but also changes at the micro-level ocular structural level can be monitored in parallel with treatment. OCT, which can detect these changes, especially those occurring at the RNFL and choroid level, in a non-invasive manner, can be a useful complementary tool in monitoring treatment response and evaluating potential ocular effects early. In this respect, it is thought that OCT can contribute to the multidisciplinary follow-up process in pediatric anemia cases.

Declarations

Ethics approval and consent to participate

The study was approved by the Van Yüzüncü Yıl University Faculty of Medicine Clinical Research Ethics Committee with decision number 03 dated 27.03.2024. It was conducted in accordance with the principles of the Helsinki Declaration, and informed written consent was obtained from the families of all participants.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Authors' information

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Author Contribution

AE conceived and designed the study, participated in data interpretation, and drafted the manuscript. BA contributed to study design, data interpretation, and critical revision of the manuscript. SK contributed to the clinical evaluation of patients and interpretation of pediatric data. MM collected the pediatric clinical data, , contributed to patient follow-up and data acquisition. VY performed the ophthalmological evaluations, contributed to OCT data interpretation, and critically revised the manuscript for important intellectual content. All authors read and approved the final manuscript.

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The authors used an AI-assisted language tool to improve the readability, grammar, and overall clarity of the manuscript. All scientific content, interpretations, and final wording were reviewed and approved by the authors.

Data Availability

The datasets generated and/or analyzed during the current study are not publicly available due to institutional and participant confidentiality considerations but are available from the corresponding author on reasonable request.

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