Clinicians often encounter a situation where residual impairment in vision continue to persist despite adequate and timely treatment (full time, full spectacle correction and/or patching) of children with (ISO) ametropic or anisometropic amblyopia. A repeat evaluation of the optical media, retina and rest of the visual pathway may or may not reveal a previously unrecognised pathology. Not infrequently however, a detailed clinical re-evaluation, electrophysiological tests (ERG, VEP), color vision, perimetry etc. would reveal no abnormality. The clinicians would then wonder about the lack of vision improvement / persistent vision impairment and diagnose the patient with “residual” amblyopia.

In this investigation, we evaluated the magnitude and the prevalence of higher order aberration (HOA) in children with so called residual amblyopia using the iTraceTM (Tracey Technologies Corp., Japan). The unrecognised (and therefore uncorrected) HOAs appeared to be one of the potential causes of residual amblyopia in children with ametropic / anisometropic amblyopia.

**MATERIALS AND METHODS**

In this prospective double masked, cross sectional, observational, cohort study, cooperative children aged 6-16 years were included. The children were divided in three groups.

**Group 1**

Emmetropic children with vision 6/6 and no ocular abnormality.

**Group 2**

Ametropic children {refractive error of ≥1D [spherical equivalent (SE)]} with best corrected vision ≥ 6/6.
**Group 3**

Children with ametropia (refractive error of ≥1D [spherical equivalent (SE)]) or anisometropia (i.e. inter eye difference ≥1D SE) and residual amblyopia (≥2 line loss of vision on logMAR chart for ametropic amblyopia or inter eye acuity difference of ≥2 lines on logMAR chart).

The children were recruited after a detailed evaluation by a masked optometrist (unaware of the results of Wavefront Analysis) and a masked Pediatric Ophthalmologist. Residual amblyopia was diagnosed in patients after one year of completing the treatment that included full refractive correction with 100% compliance, maximum conventional occlusion therapy (patching) and oral levodopa in selected cases.

An ophthalmic technician, masked to the results of the clinical examination, performed Wavefront analysis using the iTrace.

The clinical data and the Wavefront reports were submitted to the data entry operator. All the Zernicke coefficients [26 parameters each for corneal optics, internal (lenticular) optics and total optics] and RMS value of the total HOAs were entered in an excel sheet for analysis.

For each group, the mean RMS value and mean HOAs (Zernicke coefficient, order 3 to 6) were calculated and compared. For inter group comparison, P value was calculated using two tailed t test for samples with equal variance. Paired t test was used for comparison of two eyes of patients with anisometropic amblyopia.

**Sample Size Calculation**

Since we were dealing with a continuous independent variable (Z values and RMS values) we used the formula \[ N= \frac{2 (Z_{1-\alpha/2} - Z_{1-\beta})^2}{d^2}. \]

For 5% significance with 80% power of the study to detect difference of 0.25% with standard deviation of control group (\(S_c = 0.2\)) [calculated from first 20 examinations] we needed total 50.1 eyes.

**RESULTS**

We included 86 eyes of 47 consecutive children (Table 1)

The root mean square (RMS) value of the total HOA (HOA) was significantly high in amblyopic eyes compared to 1) normal eyes \((p=0.002)\), 2) ametropic eyes with normal vision and 3) the better eye of the patients with anisometropic amblyopia (Table 2).

A comparison of Zernicke coefficients of the corneal aberrations and internal (lenticular) aberrations in children with normal eyes revealed that upto 4th order, there was no statistically significant difference in internal aberrations compared with corneal aberrations. The 5th order pentafoil and all 6th order aberrations were higher for the internal optics compared to the corneal optics.
A comparison of Zernicke coefficients in children with normal vision and ametropic amblyopia demonstrate that mean 4th order tetrafoils from internal aberrations and mean 5th order pentafoils in the corneal aberrations were statistically higher in children with ametropic amblyopia.

Among the children with anisometropic amblyopia none of the 27 corneal aberrations were higher compared to the normal eyes while all the HOAs from the internal optics were significantly higher in comparison to the normal eyes (Table 3).

<table>
<thead>
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<th>Table 1</th>
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<tbody>
<tr>
<td>Normal Vision with Emmetropia (Group 1)</td>
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<tr>
<td>No of children</td>
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<td>No of eyes</td>
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<td>Mean age in years</td>
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<tr>
<th>Table 2: Root mean square (RMS) value of total HOA (HOA)</th>
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<tr>
<td>Group 1</td>
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<tr>
<td>Total HOA (RMS) [range]</td>
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<td>Standard Deviation</td>
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<th>Table 3: Comparison of HOA (internal optics) of children with anisometropic amblyopia with normal eyes</th>
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<tr>
<td>Order</td>
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DISCUSSION

HOAs are refractive errors that cannot be corrected by sphero-cylindric lenses. Although ignored for many years, they recently have become the subject of interest because of improved methods of both measurement and treatment.[2] However, the exact clinical significance of higher-order aberrations remains unclear.

Brunette et. al.3 and Kirwan et. al.2 found that higher-order aberrations were significant in childhood and decreased progressively to the third decade, after which time they increased gradually to old age. The effect of the refractive status (myopia or hyperopia) on HOA is equivocal, with some authors reporting increased HOA in myopes2,4 and others find no difference.5 However, hyperopia and cycloplegia does not seem to significantly affect the HOA.2

In this study, the higher order aberrations in children were found to be higher than what is reported for adults using the same technology. The aberrations were often lenticular in origin. The amblyopic eyes in anisometropia and isoametropic amblyopia had statistically higher amount of higher order aberrations. The difference was more pronounced in anisometropia. In isoametropic amblyopia, more ametropic eyes had higher amount of HOA than the less ametropic eyes.

Prescription of Iscription (Aberration neutralising lenses from Zeiss) led to significantly reduced total HOA in these patients. A separate study is ongoing to assess the impact of reduced total HOA with those spectacle lenses on the visual functions of amblyopic eyes.

The clinicians should be aware of possible association of HOA with amblyopia. Further studies are needed to evaluate the effect of its correction on the treatment of amblyopia.

REFERENCES