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ORIGINAL ARTICLE

EVALUATION OF HIGHER ORDER ABERRATIONS IN CHILDREN WITH UNILATERAL ANISOMETROPIC AMBLYOPIA

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ABSTRACT: OBJECTIVES: To quantify and analyse the higher order aberrations occurring in unilateral anisometropic Amblyopic eyes in our hospital. **METHODS:** An ORK WAVEFRONT ANALYZER – COAS version 1.43.2 Hartmann-Shack aberrometer was used to measure the ocular monochromatic aberrations. Amblyopic children comprising of only anisometric amblyopia were considered. **RESULT**: A total of 38 Anisometropic Amblyopes among the 63 Unilateral Amblyopic Children between 5-12 yrs. were studied. The arithmetic mean values for RMS of Total HOA in the AMBLYOPIC EYE and NORMAL EYE in ANISOMETROPIC MYOPIC AMBLYOPIA were 0.097 and 0.071 respectively. This difference was statistically significant (p=0.044).The arithmetic mean values for COMA (3,-1) and TREFOIL (3,-3) were statistically significant. **CONCLUSION:** This study indicates that among the types of unilateral anisometropic myopic amblyopia there was statistically significant relation in RMS of Total HOA, COMA (3,-1), TREFOIL (3,-3).

KEYWORDS: Higher order aberration, Wave front aberration, Anisometropic amblyopia.

INTRODUCTION: Amblyopia is defined as the best corrected VA less than 0.3 logMAR unit (i.e.<40 letters, equivalent to Snellen VA<20/40) in the affected eye, not attributable to any underlying structural abnormality of the eye or visual pathway plus a difference of at least 2 logMAR lines between the 2 eyes.

Optical aberrations occur when rays of light deviate from their desired focus point within the eye. In physical optics, light travels in waves, spreading out in all directions in a spherical pattern.

The wave front is defined as the shape of the light waves that are in phase with one another. An aberration-free optical system in an "ideal" eye has a perfect wave front, which is described as a plane perpendicular to the line of sight. However, disturbances or aberrations of this perfect wave front occur in normal eyes. Wave front aberration error may be defined as the deviation of the actual wave front from the perfect ideal wave front in the plane of the eye's exit pupil. The local slope of the wave front curve at the particular spot within the pupil is derived from the actual image displacement of the point source from foveola as it passes through the optical system of the eye as compared to the ideal/predicted image of the ideal optical system. It is quantified by calculating the root mean square (RMS) of the deviation.

Aberrations may be subdivided into low order aberrations, which can be corrected by sphero-cylindrical lenses, and higher order aberrations, which cannot. Major technological advances in the field of refractive surgery have led to the development of instruments that allow easy measurement of higher order aberrations. The most commonly used apparatus is based on the principles of Hartmann–Shack aberrometry, which measures distortions in a wave front of light emitted from the eye after it has passed through the eye's optics.

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This aberrometer uses an optical system that images the wave front located at the eye's entrance pupil into an array of microscopic lenslets that divide the beam of light exiting the eye into many smaller beams that are focused as tiny spots on a video sensor.

Monochromatic aberrations can be decomposed into Zernike polynomials (ZP) consisting of Zernike terms (ZT).Each term ZT of ZP corresponds to a specific geometric pattern of the aberration (e.g. ZT3 = astigmatism). The number (e.g. ZT3 = 0.4) next to the particular term (e.g. term ZT3) describes the amount of this particular type of aberration present. Zernike terms are grouped into orders of ZP (Second order ZP are terms 3, 4, 5). (Figure 1)

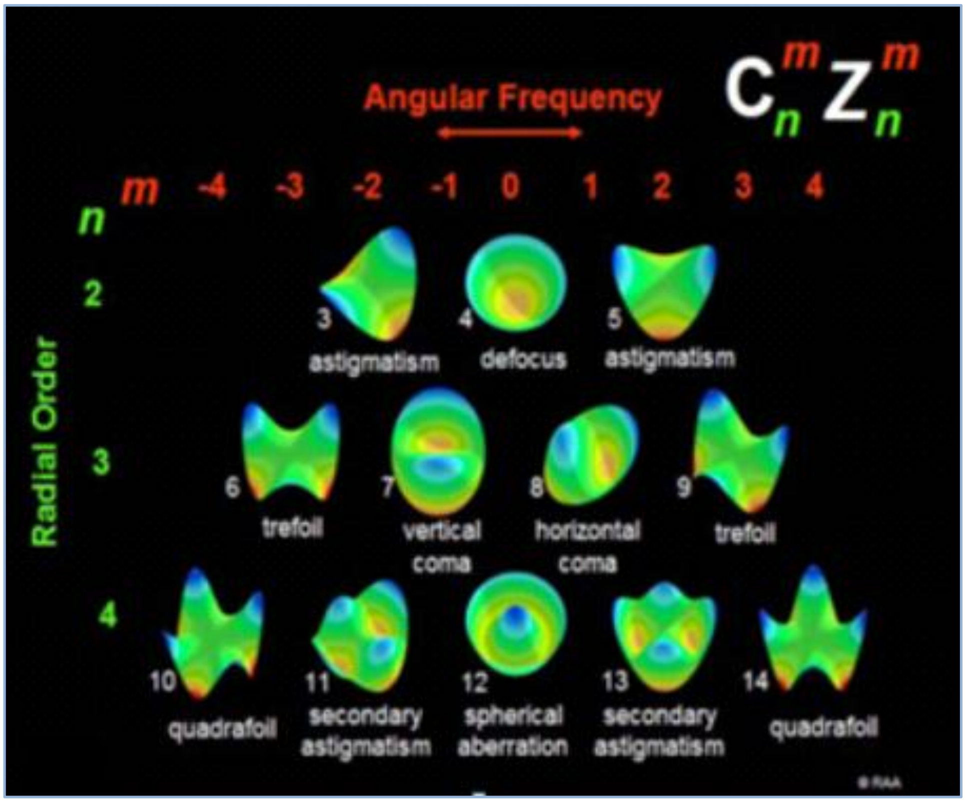

Fig 1: 3 Dimensional representation of higher order aberrations

These are mathematical expressions describing how much of what type of geometrical pattern (Each term of ZP) is contributing to the total optical (wave front) aberration. This can be thought of in a similar way, as any curve (function) in geometry can be mathematically approximated with a polynomial function (i.e., a function y = a+bx2+cx3+dx4…).

In 2011 May, Prakash G et al,[1] conducted a study to evaluate the higher order aberrations and resultant bilateral wave front patterns in pediatric patients with idiopathic amblyopia at Cornea and Refractive Surgery Services, Rajendra Prasad Centre for Ophthalmic Sciences, All India Institute of Medical Sciences, Ansari Nagar, New Delhi, India. It was a cross sectional observational trial. They examined around 17 children. Consecutive patients of previously diagnosed idiopathic amblyopia underwent wave front analysis on Zyoptix platform (Bausch and Lomb, Rochester, NY, USA). The mean age was 9±3 years.

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There was no significant difference in comparison with means for the Zernike coefficients between normal and amblyopic eye. However, interrelation between Zernike coefficients, which is responsible for their interaction leading to difference in visual function, was different between amblyopic and fellow eyes. This was noticed using stepwise regression analysis. Predicting variables and R2 (r squared) values for each Zernike polynomial were calculated. The sets of significantly predicting coefficients were different in most patients, with only seven common pairs and 42 dissimilar dependent-predictor sets. Maximum difference in the R-squared values between amblyopic and normal (fellow) eyes was seen with coma-like and trefoil-like aberrations (third order and fifth order terms). It seems a strong possibility that a subset of 'idiopathic' amblyopia may be associated with loss of symmetry in wave front patterns of the two eyes. (To evaluate the higher order aberrations and resultant bilateral wave front patterns in pediatric patients with idiopathic amblyopia, Acta Ophthalmol. 2011 May; 89(3): e257-62).

In 2011 May, Alió JL et al.[2] conducted a study to provide an overview of the visual outcomes after pediatric refractive surgery in Anisometropia Amblyopia and to analyze the relationship of these outcomes with age and type of refractive surgery. Only studies reporting individual data of pediatric cases (age 1 to 17 years) undergoing photorefractive keratectomy (PRK), laser epithelial keratomileusis (LASEK), and LASIK were included. A total of 15 articles including data from a total of 213 amblyopic eyes were considered: LASIK in 95 eyes and surface ablation in 118 eyes. Changes in uncorrected (UDVA) and corrected distance visual acuity (CDVA) were investigated as well as their relation with age and ablation type. A significant increase in log MAR UDVA and CDVA was found in the overall sample of amblyopic eyes after surgery ($P<.001$). A significant correlation was found between age and preoperative CDVA ($r=0.34$, $P<.001$) as well as between age and the change in CDVA after surgery ($r=-0.38$, $P<.001$).

The change in UDVA was significantly superior for eyes undergoing surface ablation compared to those undergoing LASIK ($P=.04$). Corneal haze was the predominant complication, which was reported in 5.3% of LASIK cases and 8.5% of surface ablation cases. Laser refractive surgery is an effective option for improving the visual acuity in children with an amblyopic eye in association with Anisometropia. (Pediatric refractive surgery and its role in the treatment of amblyopia: meta-analysis of the peer-reviewed literature. J Refract Surg. 2011 May; 27(5):364-74).

In 2010, Zhao PF et al,[3] conducted a study to evaluate the wave front aberrations in children with amblyopia at Beijing Tongren Eye Center, Beijing Tongren Hospital, Capital Medical University; Beijing. The Waves can Wave front System (VISX, USA) aberrometer was used to investigate four groups of children under dark accommodation and ciliary muscle paralysis. There were 45 cases in the metropic group, 87 in the amblyopic group, 92 in the corrected-amblyopic group and 38 in the refractory amblyopic group. One-way analysis of variance (ANOVA), t-test and multivariate linear regression were used to analyze all the data. Third order to 6th order aberrations showed a decreasing trend whereas in the higher order aberrations the main ones were 3rd order coma (Z(3)(-1)-Z(3)(1)), trefoil (Z(3)(-3)-Z(3)(3)) and 4th order aberration (Z(4)(0)); and 3rd order coma represented the highest percentage of all three main aberrations.

Within 3rd order coma, vertical coma (Z (3) (-1)) accounted for a greater percentage than horizontal coma (Z (3) (1)). Significant differences of vertical coma were found among all clinical groups of children: vertical coma in the amblyopic group (0.17+/-0.15) was significantly higher than in the metropic group (0.11+/-0.13, $P<0.05$).

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In addition, the vertical coma in the refractory amblyopic group (0.19+/-0.15) was higher compared with the metropic group (P<0.05), the 5th order aberration (0.11+/-0.08) was also significantly higher than in the metropic group (0.07 +/- 0.04, P < 0.05). No significant difference was found in vertical coma and 5th order aberration between the corrected-amblyopic group (0.13+/- 0.11) and metropic group (0.07+/-0.04) (P>0.05). (To evaluate the wave front aberrations in children with amblyopia Chin Med J (Engl). 2010 Jun; 123(11):1431-5.)

In 2010 Jan, Plech AR et al,(4) (Vissum/Instituto Oftalmológico de Alicante, Universidad de Alicante, Alicante - Spain) investigated the amount, type, and role of corneal higher order aberrations in both isotropic and Anisometropic amblyopic adult patients. Around 125 eyes of 78 patients with age ranging from 18 to 67 years (30 patients with unilateral amblyopia, 17 with bilateral amblyopia, and 31 normal eyes considered as the control group) were included. Corneal topographic and aberrometric analysis was done with the CSO system. Higher amounts of primary coma were found in isometropic eyes (0.25µ Anisometropic vs 0.43µ isometropic, p=0.09).

It was concluded that in unilateral and bilateral amblyopia, lower order aberrations are the main refractive factors leading to amblyopia. Higher order aberrations could have a bilateral amblyogenic effect in those cases where isometropia is present. (The amount, type, and role of corneal higher order aberrations in both isotropic and Anisometropic amblyopic adult patients Eur J Ophthalmol. 2010 Jan-Feb; 20(1):12-20.)

In 2010 March, Prakash G et al,(5) conducted a study to evaluate the higher order aberrations and resultant bilateral wave front patterns in pediatric patients with idiopathic amblyopia at Cornea and Refractive Surgery Services, Rajendra Prasad Centre for Ophthalmic Sciences, All India Institute of Medical Sciences, Ansari Nagar, New Delhi, India. In this cross sectional observational trial, seventeen consecutive patients of previously diagnosed idiopathic amblyopia underwent wave front analysis on Zyoptix platform (Bausch and Lomb, Rochester, NY, USA).

The mean age was 9+/-3 years. There was no significant difference in comparison with means for the Zernike coefficients between normal and amblyopic eye. However, interrelation between Zernike coefficients, which is responsible for their interaction leading to difference in visual function, was different between amblyopic and fellow eyes. This was noticed using stepwise regression analysis. Predicting variables and R2 (r squared) values for each Zernike polynomial were calculated. The sets of significantly predicting coefficients were different in most patients, with only seven common pairs and 42 dissimilar dependent-predictor sets.

Maximum difference in the R-squared values between amblyopic and normal (Fellow) eyes was seen with coma-like and trefoil-like aberrations (Third order and fifth order terms). Conclusion: It seems a strong possibility that a subset of 'idiopathic' amblyopia may be associated with loss of symmetry in wave front patterns of the two eyes. (The higher order aberrations and resultant bilateral wave front patterns in pediatric patients with idiopathic amblyopia. Acta Ophthalmol. 2010 Mar 12-Epub.)

In 2009 March, Yu FJet al,(6) (West China Hospital, Sichuan University, Chengdu, China) compared the distribution of ocular higher-order aberrations in control group and refractive Amblyopia group .The higher-order aberrations were measured in 74 eyes using Allegro Wave Analyzer. Yu FJ, Song HY, Liu LQ, Deng YP, Wang L evaluated that RMS4, RMS5, RMS6 and RMS3 in Amblyopia were all significantly greater than those in control group. RMS3 was the dominant higher-order aberration in the two groups. Coma and Y-axis coma had significant differences in the two groups.

It was concluded that higher-order aberrations had significant associations with Amblyopia Coma; particularly y-axis coma plays an important part in the corrected vision.(The distribution of ocular higher-order aberrations in control group and refractive Amblyopia group Sichuan Da Xue, Xue Bao, Yi Xue Ban. 2009 Mar; 40(2):311-3.)

In 2009 May, Agarwal A et al,[7] evaluated a study on whether uncompensated higher order aberration profile, or aberropia be responsible for subnormal best corrected vision and pseudo-amblyopia. They hypothesized that abnormally increased and uncompensated higherorder aberration profile in certain cases may limit the amount of best corrected visual acuity to subnormal levels and produce a pseudo-amblyopia like picture which was termed aberropia. IMPLICATIONS OF THE HYPOTHESES: Understanding of uncompensated higher order profiles leading to loss of BCVA, or aberropia, would be a paradigm shift in understanding of the role of higher order aberrations on visual function. With improvement in diagnostic and treatment methods, these patients with a subnormal vision may be treated to achieve their maximum visual potential. (Med Hypotheses. 2009 May; 72(5):574-7. Epub 2009 Feb. 12.)

In 2008, March, Caitriona kirwan et al.[8] (The Children's University Hospital, Dublin, Ireland) quantified and characterized the higher order aberrations in children with amblyopia. 30 children aged between 6 & 17 were considered. 15 children had strabismic amblyopia and 15 children had Anisometropic amblyopia. Caitriona kirwan & Michael o, keefe evaluated that higher order aberration measured with iTrace Visual Function Analyzer (Tracey Technologies, Houston, TX) are similar in amblyopic eyes due to squint and anisometropia & normal fellow eyes. Unlike lower order aberrations such as sphere and cylinder, higher order aberrations are unlikely to play a role in the development of amblyopia. (To quantified and characterized the higher order aberrations in children with amblyopia J Pediatr Ophthalmol Strabismus. 2008 Mar-Apr; 45(2):92-6.)

The Present Study is carried out in this Hospital with the following Objectives:

- To quantify &characterize the higher order aberrations occurring in Unilateral Amblyopic eyes with Anisometropic Amblyopiain our hospital.
- To assess the burden of Amblyopia in non-compliant children with amblyopia.
- To help clinicians in a better understanding on the management of Amblyopia by treating the HOA through refractive surgeries, if HOA proves to be an amblyopiogenic factor.
- To motivate the healthcare professionals in the effective management of Amblyopia.

MATERIALS AND METHODS:

Study Population: Children who attended our outpatient clinic, between the ages of 5- 12 years from August 2012 to July 2013.

Total of 63 Unilateral Amblyopes .Fourteen of the reported cases were excluded. From the remaining case 38 had Anisometropic Amblyopia.

Inclusion Criteria:

- Amblyopic children comprising of only anisometropic amblyopia.
- Both males and females are considered.
- Children between 5-12 years are considered.
- Unilateral amblyopes.

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Exclusion Criteria:

- Patients undergoing treatment for amblyopia.
- Patients with any organic lesion in fundus.
- Patients who had undergone amblyopic treatment before.
- Patient with refractive errors more than 6 D.

Instrument: The best visual acuity was determined prior to testing with Snellen's chart, following which binocular vision was tested and severity of amblyopia was assessed.

An Optimized Refractive Keratometer (ORK) WAVEFRONT ANALYZER– Complete Ophthalmic Analysis System (COAS) version 1.43.2 Hartmann-Shack aberrometer (Schwind Technologies, Germany) was used to measure the ocular.

Statistical analysis was performed using the Student's paired t test. A p value of less than 0.001 was deemed statistically significant.

RESULTS: The arithmetic mean values for the RMS in the amblyopic and normal eye were 0.096 and 0.073 µ, respectively. This difference was statistically significant ($p<0.001$). This was consistent with the study by Zhao PF et al,(3) Yu FJ et al,(6) Plech AR et al,(4) L.S. Gray et al,(9) but different from the study carried out by Prakash G et al,(1) Caitriona Kirwan et al,(8) Namrata Sharma et al.(10)March, Caitriona kirwan & Michael o, keefe, Saxena R et al.[4] in which total HOA root mean square (HORMS) values were higher in the normal fellow eye than in the amblyopic eye. The arithmetic mean values for COMA (3,-1) in the amblyopic and normal eye were 0.121 and 0.07 µ respectively. This difference was statistically significant ($p<0.001$). This was consistent with the study by Zhao PF et al,[2] Yu FJ et al.[5] and Plech AR et al.[3] but different from the study carried out by Prakash G et al.[1] in which the 3rd order coma was 3.4 times higher in the normal eye.

The arithmetic mean values for TREFOIL (3,-3) in the amblyopic and normal eye were 0.102 and 0.074 µ, respectively. This difference was statistically significant ($p<0.001$). This was consistent with the study by Zhao PF et al,[2] L.S. Gray.[8] but different from the study carried out by Prakash G et al.[1] in which trefoil was 1.23 times higher in the normal eye. The arithmetic mean values for SPHERICAL (4,0). in the amblyopic and normal eye were 0.088 and 0.67µ respectively. This difference was statistically significant ($p<0.001$). This was consistent with the study by Yu FJ et al,[5] but was different from the study carried out by Zhao PF et al,[2] Plech AR,[3] and L.S. Gray.[8] Hence there were statistically significant relation in RMS of Total HOA, COMA (3,-1), TREFOIL (3,-3) and SPHERICAL (4,0). The mean arithmetic values for the remainder polynomials showed no statistically significant difference between the amblyopic eyes and the healthy fellow eyes. (Graph 1, Table 1)

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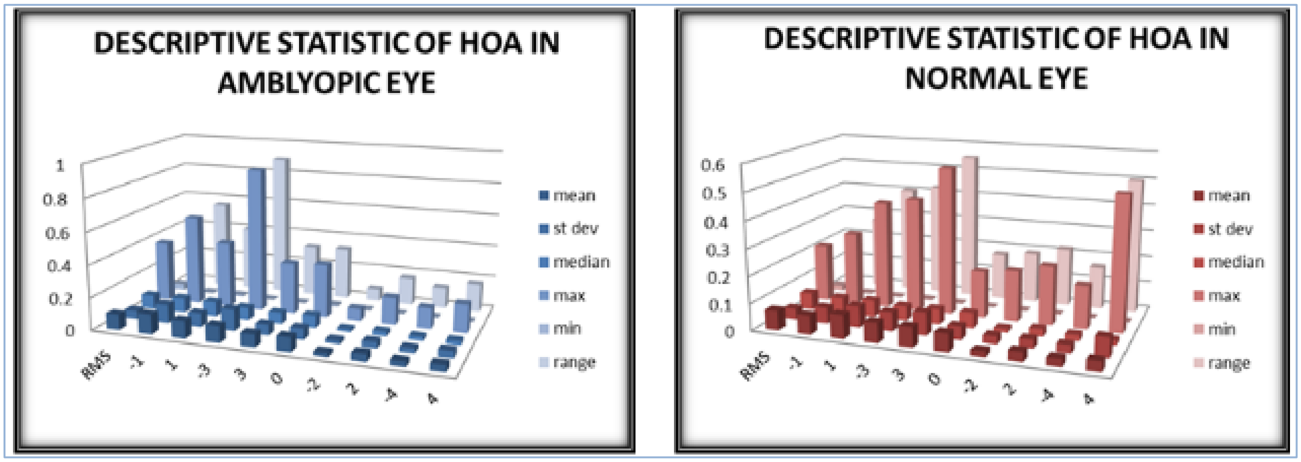
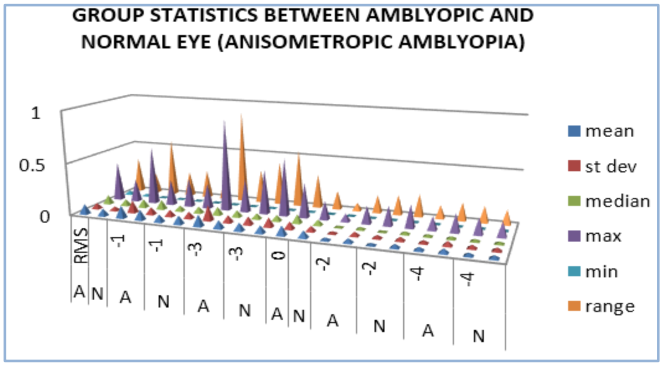


Graph 1: Group statistics of HOA in amblyopic and normal eye

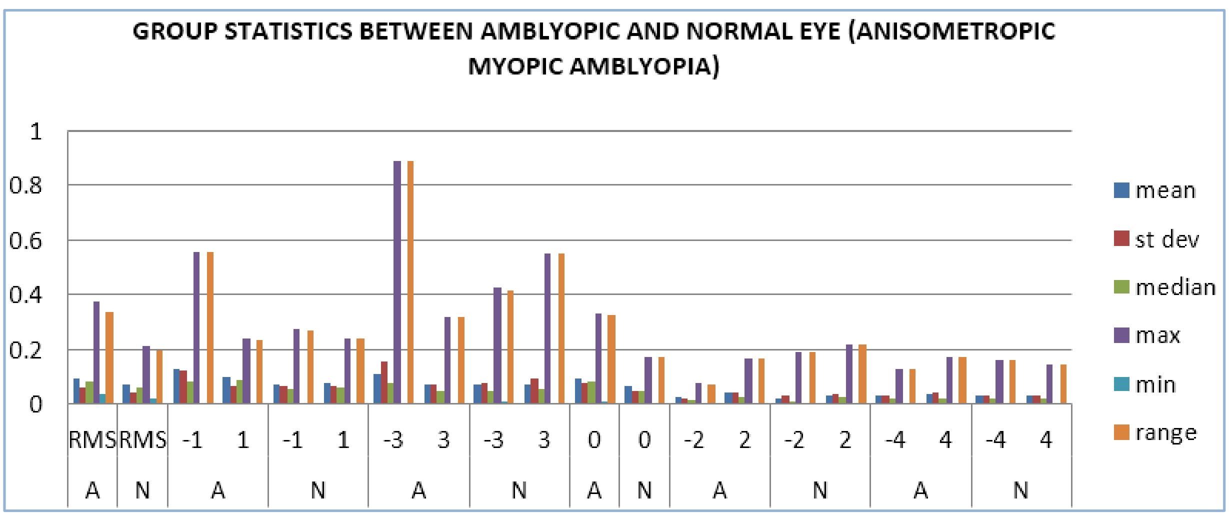
Hence third order to fourth order showed a decreasing trend which was more significant in the amblyopic eye than in healthy fellow eye, where the decreasing trend pattern was not clearly met. The main Higher Order Aberrations (HOA) was mean of Total HOA, Vertical Coma (3,-1), Vertical Trefoil (3,-3) and Spherical (4, 0) in the amblyopic eye. In this the highest percentage was shown by Vertical Coma (3,-1), 19%. Vertical coma was higher in the amblyopic eye by 1.35 times than the normal eye. Vertical coma was higher than horizontal coma by 1.12 times.

The arithmetic mean values for RMS of Total HOA in the AMBLYOPIC EYE and NORMAL EYE in ANISOMETROPIC AMBLYOPIA were 0.095 and 0.07 respectively. This difference was statistically significant ($p<0.001$). The arithmetic mean values for COMA (3,-1) in the AMBLYOPIC EYE and NORMAL EYE in ANISOMETROPIC AMBLYOPIA were 0.118 and 0.071 respectively. This difference was statistically significant ($p<0.001$). The arithmetic mean values for TREFOIL (3,-3) in the AMBLYOPIC EYE and NORMAL EYE in ANISOMETROPIC AMBLYOPIA were 0.11 and 0.076 respectively. This difference was statistically significant ($p<0.001$). The arithmetic mean values for SPHERICAL (4, 0) in the AMBLYOPIC EYE and NORMAL EYE in ANISOMETROPIC AMBLYOPIA were 0.049 and 0.032 respectively. This difference was statistically significant ($p<0.001$). The mean arithmetic values for the remainder polynomials showed no statistically significant difference between the amblyopic eyes and the healthy fellow eyes. (Graph 2, Table 2)



Graph 2: Group statistics between nisometropic amblyopic eye and normal eye

The arithmetic mean values for RMS of Total HOA in the AMBLYOPIC EYE and NORMAL EYE in ANISOMETROPIC MYOPIC AMBLYOPIA were 0.097 and 0.071 respectively. This difference was statistically significant ($p<0.001$).The arithmetic mean values for COMA (3,-1) in the AMBLYOPIC EYE and NORMAL EYE in ANISOMETROPIC MYOPIC AMBLYOPIA were 0.127 and 0.073 respectively. This difference was statistically significant ($p<0.001$). The arithmetic mean values for TREFOIL (3,-3) in the AMBLYOPIC EYE and NORMAL EYE in ANISOMETROPIC MYOPIC AMBLYOPIA were 0.112 and 0.073 respectively. This difference was statistically significant ($p<0.001$). The mean arithmetic values for the remainder polynomials showed no statistically significant difference between the amblyopic eyes and the healthy fellow eyes. (Graph 3, Table 3)



Graph 3: Group statistics between anisometropic amblyopic eye and normal eye

In the ANISOMETROPIC HYPERMETROPIC amblyopia there was no significant statistical difference between amblyopic and normal eye (Table 4)

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DISCUSSION: Amblyopia is the most important cause of unilateral visual impairment in children and adults under 60 years and accounts for 50% to 73% of all such vision loss. Overall, global estimates of the prevalence of amblyopia range from 0.20% to 6.2%. In the first phase of our study, children from, around ten schools, between grades II and VIII were screened for refractive errors and strabismus, in a period of three months. Among the 3721 students screened it was found that 278 children had significant refractive errors, 21 children had strabismus and 16 of the children had both. Amblyopia was found in 31 of them, which accounted for 0.8% of the screened children. This result is consistent with the results of population-based Multi-ethnic Pediatric Eye Disease Study (MEPEDS) and Baltimore Pediatric Eye Disease Study (BPEDS) in which, Friedman et al. reported the BEPDS findings on 2546 children, with amblyopia, prevalence rates of 1.8% and 0.8%, in Caucasian and African-American children, respectively, in 2009. These children were referred to the Pediatric Ophthalmology Department of our hospital. Among them 28 children turned up at the Hospital, of which only 19 were taken up for the study.

Overall, global estimates of the prevalence of strabismus in children and teenagers range from 0.13% to 4.7%, respectively. The population-based Multi-ethnic Pediatric Eye Disease Study (MEPEDS) and (Baltimore Pediatric Eye Disease Study BPEDS) is evaluating the prevalence of strabismus in 12,000 children of 6-72 months from 4 ethnic groups—African American, Asian American, Hispanic/Latino, and non-Hispanic Caucasian. In 2009, Friedman et al. reported the BEPDS findings on 2546 children, with strabismus prevalence rates of 3.3% and 2.1% in Caucasian and African-American children, respectively.

CONCLUSIONS: This study proved that among the types of unilateral amblyopia reported at our hospital during the study period there were statistically significant relation in RMS of Total HOA, COMA (3,-1), TREFOIL (3,-3) and SPHERICAL (4, 0) especially among Myopic Amblyopes. In conclusion our findings indicate that there is significant in-between eye difference of HOA in this group of Myopic Amblyopic patients. Our findings support the hypothesis of aberropia.

RECOMMENDATIONS: Further research on the distributions of HOA in a specific group of amblyopes is necessary. Although lower order aberrations major factors determining the quality of the retinal image, higher order aberrations also need to be considered in especially among Myopic Amblyopic eyes as their effects are significant. There is a great need for awareness about the importance of HOA in the treatment of non-compliant cases of amblyopia, among the ophthalmologists. To overcome this problem multiple study trials should be conducted in various hospitals and the success rates in the treatment of amblyopia should be further increased by treating HOA with wavefront guided optical lenses or wavefront laser ablation.

Thus we can minimize the non-compliant cases of amblyopia and also provide a good quality of life to the patients and also reduce the health care cost due to Amblyopia. More research is also needed on the impact of interactions between higher order aberrations and the visual performance. Knowing which sets of Zernike terms could improve or reduce visual performance could bring new discoveries, which can clarify the current findings in studies of HOA. More research is needed on the impact of neuroadaptability to different types of higher order aberrations in the span of time in different age groups.

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We would suggest doing this in a group of therapy resistant amblyopic patients who had a history of early discovery of amblyopia, high treatment compliance and yet a sustained amblyopia. Another interesting group to study would also be the idiopathic amblyopes. Because never the less we still believe that presence of higher order aberrations in an individual with amblyopia can disturb the visual performance in such a way that it can be clinically significant.

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