Original Article

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Pattern of Anisometropia, Management and Outcome of Anisometropic Amblyopia

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ABSTRACT

Purpose: Amblyopia is a frequent cause of monocular visual impairment in children. It can be unilateral or bilateral reduction of best corrected visual acuity associated with decrement in visual processing, accommodation, motility, spatial perception or spatial projection. Anisometropia is an important risk factor for amblyopia that develops when unequal refractive error causes the image to be blurred in the critical developmental period and central inhibition of the visual signal originating from the affected eye associated with significant visual problems including aneisokonia, strabismus, and reduced stereopsis.

Methods: It is a prospective hospital-based study of newly diagnosed of anisometropic amblyopia seen at the pediatric clinic of Chittagong Eye Infirmary & Training Complex. There were 50 anisometropic amblyopia subjects were examined. All the patients diagnosed with refractive amblyopia between 3 to 13 years, without previous amblyopia treatment, and whose parents were interested to participate in this study were included. Patients diagnosed with strabismic amblyopia and other ocular anomalies were excluded. Patients were first corrected with the best correction for a month. When the VA in the amblyopic eye did not improve over month, then occlusion treatment was started. Occlusion was given daily for 6-8 hours (full time) together with vision therapy. The occlusion was carried out for 3 months.

Results: In this study about 4 (8%) subjects had anisometropia from myopia, 9 (18%) from hyperopia, 37 (74%) from astigmatism. The initial mean visual acuity was 0.74 ± 0.39 LogMAR and after intervention of amblyopia therapy with active vision therapy mean visual acuity was 0.34 ± 0.26 LogMAR. About 47 (94%) of subjects improved visual acuity at least two lines. The depth of amblyopia associated with type of anisometropic refractive error and magnitude of Anisometropia ($p<0.005$). In this study, only 5 (10%) mild amblyopia, 32 (64%) moderate and 13 (26%) severe amblyopia were found. Binocular function also decreases with magnitude of Anisometropia.

Conclusion: Anisometropic amblyopia is a most important factor in pediatric age group because it can lead to visual impairment. Occlusion therapy with at least one-hour active visual activity practiced out of school hours was effective in anisometropic amblyopia who were diagnosed at the age of 8 years and below.

Keywords: Refractive error, anisometropia, amblyopia, strabismic amblyopia.

Introduction

Amblyopia is a frequent cause of monocular vision loss in children. A difference in refractive error between the two eyes (anisometropia) is the leading cause of amblyopia now a day's[1]. It is the only identifiable amblyogenic factor in 37% of cases and present concomitantly with strabismus in an additional 24% of clinical populations[2].

Studies examining the association of anisometropia and amblyopia in young children found a significant association between the two, with a low prevalence of amblyopia overall 1.5%–2.6% and part of it 24% - 37% due to anisometropia[3]. Anisometropic amblyopia is a decrease in the best-corrected VA in one eye, resulting from considerably different refractive errors in the patient's two eyes[4]. Anisometropic amblyopia is

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a common cause of amblyopia that has an estimated prevalence in the pediatric population ranging from 2% to 5%. The prevalence of Anisometropia in Asian region had been reported from 1.6% to 11.2% in children and young students[7].The prevalence of anisometropia in childhood is complicated further as it may be population-specific, with reports of a prevalence of 1.6% in 6-year-old children in Australia, 14.67% in 4 to 13 year old children in American and Indians, and 9.9% in 7- to 18-year-olds children in Taiwan. A lower prevalence of anisometropia of 5.8% was reported in children in the United States aged 12 to 15 years where anisometropia was associated with myopic and hyperopic refractive errors[9]. Previous study reported that an anisometropia prevalence of 3.1% in school children. Another study revealed an anisometropia prevalence of 14.4% in Singapore. A study in Japan found a small increase in the prevalence of spherical anisometropia rising from 1.43% at 6 years of children and 3.14% at 11 years of children[11]. The appropriate timing of treatment to successfully prevent anisometropic amblyopia not only depends on the patient's age but also on the type and degree of anisometropia that is present. Usually refractive correction is a necessary component of the treatment of anisometropia amblyopia and is frequently prescribed together with occlusion or penalization of the preferred eye[5]. Despite an excellent therapeutic success rate, it is difficult to predict whether the improvement would sustain after stopping amblyopia treatment. But in previous few study shows that mild and moderate anisometropia is able to treat with spectacle correction alone.

Bangladesh is a developing country of the world and having a population with about 16 million and out of them above three million composite 5-13 years which constitute 17% of total population of country. About 3.4% of these age groups are suffering from amblyopia[6]. This statistic is alarming for our raising school going children and needs a vast study in this issue.

Methodology

This was a prospective hospital based cross sectional study which included 50 newly diagnosed anisometropic amblyopia patients, had difference of more than ± 2.00Ds diopter recruited from the pediatric clinic of Chittagong Eye Infirmary & Training Complex (CEITC). All patients were aged between 5 to 13 years. Patient who had significant heterophoria, strabismus, previous surgery, pathological myopia, developmental delay, ocular trauma and whose parents who were not interested to participate in the study were excluded.

There were 50 anisometropic amblyopia children examined & questionnaire was performed. The information regarding age, gender, problems of the eye, vision and any previous modality of treatment etc, were recorded on a well designed proforma by interview schedule with the children's and parents of the children in the clinic. Anisometropia was classified according to the difference of refractive error between the two eyes. According to previous study refractive error difference of +1.00D for hyperopic correction, -3.00D difference for myopia and 1.50D difference for astigmatism considered as anisometropia in this study[7].

Clinical Examination

Uncorrected Visual Acuity (UCVA) and Best Corrected Spectacle Visual Acuity (BCSVA) were taken with the help of LogMAR visual acuity charts. Patient who was not responsive with LogMAR chart, VA was test with the help of Snellen chart. For statistical analysis all Snellen acuities were converted into Log MAR equivalents. Pinhole vision was also taken in both eyes with visual acuity worse than 6/6. All patients were observed for dry refraction and wet refraction with the streak retinoscope under cycloplegic eye drops. Cycloplegic refraction was carried out where required followed by subjective refraction after 3 days. Subjective refraction was done with the help of trial set for post mydriatric test. All children were evaluated under slit lamp to see any abnormality in the anterior segment and funduscopy were performed in all the cases with the help of direct ophthalmoscope. Extra ocular movements were assessed in all cardinal gazes. Near point of convergence (NPC) and near point of accommodation (NPA) test were also performed in all cases with the help of RAF ruler. Positive fusional vergence (PFV) was performed with the help of prism bar at near and distance. Eye alignment were assessed by cover uncover

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test. Stereopsis was evaluated with TNO. Contrast sensitivity were examined with 10% Beily Lovie Low contrast chart both uncorrected and corrected condition. Visuoscopy were done to evaluate fixation pattern by the help of ophthalmoscope of study patients.

Intervention

The patients were prescribed eyeglasses. They were provided with monthly patching diaries with vision therapy such as drawing, playing video games, watching TV etc, where the eye to be patched and the prescribed number of hours were written. The better eye was patched by the parents to be brought back at the next follow-up visit. If the children had no previous history of wearing glasses then the correction and occlusion therapy was prescribed followed by after 1 month. If patient was improving with glass alone occlusion therapy was not prescribed.

Follow-up Visits

Monthly follow-up visits were conducted for 3 months. First visit was after 1-month completion with spectacle and another was after 2 months with occlusion therapy. At each visit, BCVA, Fusional vergence, near point of accommodation and Contrast sensitivity were measured first in the amblyopic eye, then in the fellow eye. Short acting cycloplegic refraction was measured where required.

Data Management & Analysis

Statistical analysis was performed with SPSS 16.0. Frequency tables and cross tabulation tables were used to describe the data. For statistical tests the mean and standard deviation of present Best Corrected Visual Acuity (BCVA), Follow Up (F/U) of Visual Acuity (VA), present Best Corrected Contrast Sensitivity (BCCS), F/U of Contrast Sensitivity (CS) and spherical equivalent of both eyes was measured. The right and left eye were analyzed separately since refractive error between two eyes was independent. Effect of age on anisometropic amblyopia was determined by chi square test and student t test. Difference between anisometropia groups were compared and odds ratios with their corresponding 95% confidence interval were calculated. Graphical presentation of data was done with the help of Microsoft Excel sheet.

Result

Demographic Information of Study Children

50 Children were involved in this study of which the age of the children ranged from 5 to 13 years with a mean age of 10.02 years and standard deviation of ± 2.16. Among the total children, 30 (60%) were boys and 20 (40%) were girls. About 7 (14%) patient's education was nursery to class two, 25 (50%) had three to class five and 18 (36%) had secondary education. All patients followed up for at least 3 months. No patients dropped out of the study.

Magnitude of Anisometropic Refractive Error

In this study, 9 (18%) children had Hypermetropia, 4 (8%) had Myopia, 10 (20%) had compound Astigmatism, 19 (38%) had compound Myopic Astigmatism, 3 (6%) had simple Myopic Astigmatism, 3 (6%) had mixed Astigmatism and 2 (4%) had simple Hyperopic Astigmatism (Figure- 01).

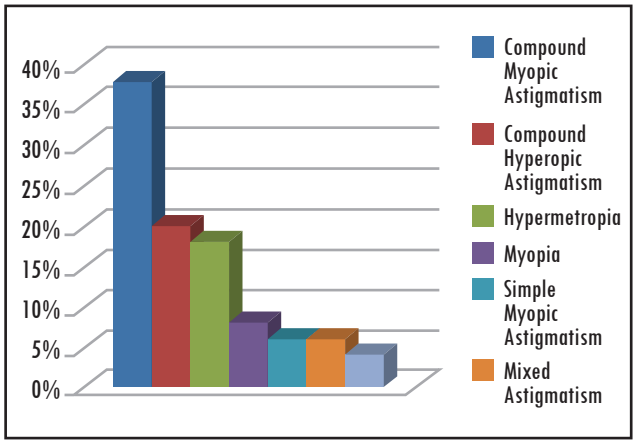

Figure- 01: Magnitude of Refractive error among the patient

The average mean spherical equivalent refraction in the amblyopic eye was +2.08D (range +0.75 to +14.0D) in hyperopia and -2.44D (range -1.00 D to -14.75D) in myopia. In sound eye mean wet refraction was -0.36± 4.77 diopters spherical equivalent ranging from (-0.25 D to -12.00D) in myopia and (0.00D to+10.25 D) in hypermetropia (Figure 02). The absolute value of mean difference in spherical equivalent refraction between the two eyes 4.08 D (range 1.00D to 12.00D) (Figure 03)

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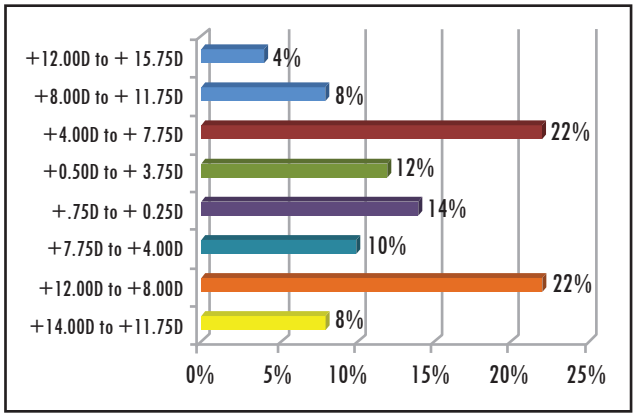


Figure - 02: Percentage distribution of refractive error of Amblyopic eye

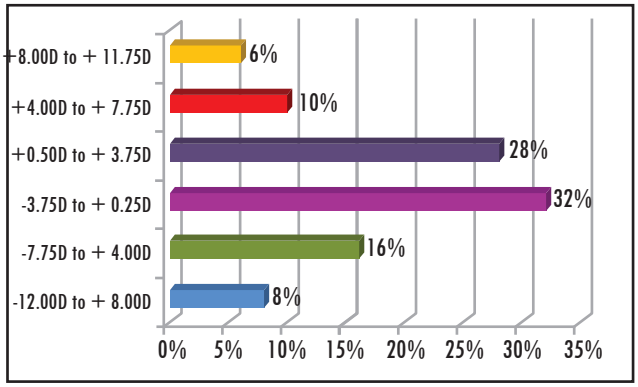


Figure - 03: Percentage distribution of refractive error of Sound eye

In this study, 29 (58%) children had bilateral amblyopia, and 21 (42%) had unilateral amblyopia. Among them 5 (10%) had mild amblyopia, 32 (64%) had moderate and 13 (26%) had severe amblyopia. The mean and standard deviation of present average visual Acuity was 0.7392 ± 0.387 LogMAR and after intervention of amblyopia therapy with vision therapy mean and standard deviation of visual Acuity was 0.33 ± 0.26 LogMAR (Figure 04).

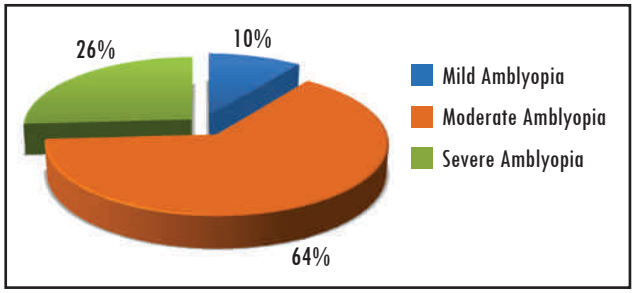


Figure - 04: Status of amblyopia among the subjects

The base line best corrected mean visual acuity (BCVA) was 0.7392 ± 0.387 LogMAR unit in amblyopic eye. The amblyopic eyes had a mean final visual acuity 0.33 ± 0.26 log MAR. The best corrected mean visual acuity was 0.1772 ± 0.2498 logMAR unit in the better eye. The better eye had mean final visual acuity 0.06 ± 0.14. (Table-01)

Effect of amblyopia increased in older children more. Marked increase of moderate and severe amblyopia more in older children aged more >8years shown in table 02. Association between age and amblyopia was statistically significant ($p<0.05$).

Table - 01: Percentage distribution of best corrected visual acuity (BCVA)

Visual Acuity Range	Amblyopic Eye	Non-amblyopic Eye
0.0 - 0.28	1 (2%)	34 (68%)
0.3 - 0.58	17 (34%)	12 (24%)
0.6 -0.88	18 (36%)	3 (6%)
0.9 - 1.08	8 (16%)	1 (2%)
1.3 - 1.8	6 (12%)	0 (0%)
Total	50 (100%)	50 (100%)

Table - 02: Percentage distribution of degree of amblyopia according to age group

Age Group	Severe	Moderate	Mild
5 year to 7 year	1 (2%)	3 (6%)	2 (4%)
8 year to 10 year	8 (16%)	14 (28%)	0 (0%)
11 year to 13 year	4 (8%)	15 (30%)	3 (6%)

Binocular Function in Anisometropia

Near point of accommodation in the amblyopic eyes decreased with magnitude of Anisometropia. In present study near point of accommodation in amblyopic eye were 8 (16%) normal, 16 (32%) reduced, 14 (28%) defective and 12 (24%) absent. In sound eye near point of accommodation were 35 (70%) normal, 7 (14%) reduced, 6 (12%) defective and 2 (4%) absent (Table 03).

Table -03: Near Point of Accommodation of the amblyopic eye and sound eye

Range of NPA	Amblyopic eye	Sound eye
Normal	8 (16%)	35 (70%)
Reduced	16 (32%)	7 (14%)
Defective	14 (28%)	6 (12%)
Could not be measured	12 (24%)	2 (4%)

Other binocular function such as fusion, suppression, stereopsis decreases along with the level of Anisometropia magnitude increased. Present study found that larger degree of anisometropia result decrease in fusional insufficiency when the anisometropia 3.00D to 6.00 D in both hyperopia and myopia. Fusion decreased at near more than distance. Mean fusion at near were 25.22± 8.45 and at distance 13.96± 4.94. (Figure 05 & Figure 06).

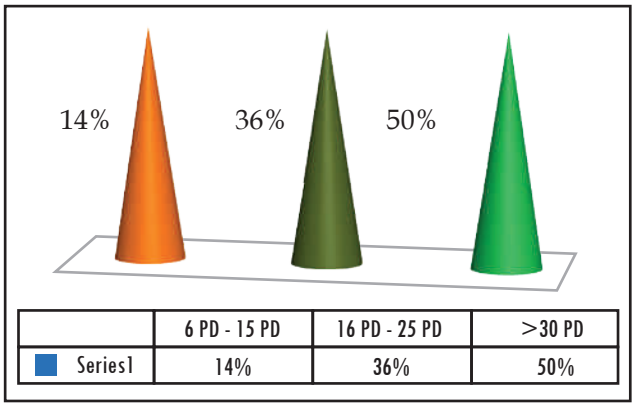


Figure - 05: Distribution of fusional vergence at near

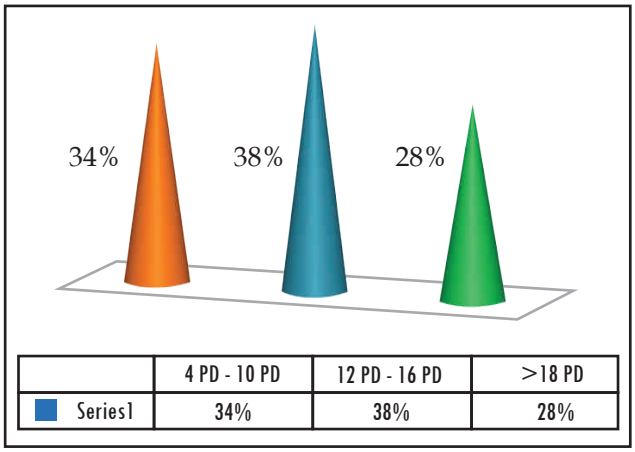


Figure - 06: Distribution of fusional vergence at distance

The suppression and stereopsis function were changed significantly as the degree of anisometropia varies. With 1 D to 3D of hyperopic anisometropia demonstrated BSV. The number of subjects showing BSV decreased with 3D to 6D of hyperopia. There was statistical change between the 1-3 D hyperopia with 3 to 6D hyperopic anisometropia. With -1 D to -2d myopia were showing BSV normal and -3 to >-6.0D myopia shows marked decrease of BSV. Among 50 patient 13 (26%) had no suppression at near, 17 (34%) had right eye suppression and 20 (40%) had left suppression (Figure 05). There were 10 (20%) children had no suppression at distance, right eye suppressed in 19 (38%) and left eye suppressed in 21 (42%) at distance (Table 04).

Table-04: Percentage of suppression at near & distance

BSV range	At Near	At Distance
BSV	13 (26%)	10 (20%)
Right suppression	17 (34%)	19 (38%)
Left suppression	20 (40%)	21 (42%)

Eccentric Fixation

The eccentricity of fixation had a very high correlation (p>.01) with the visual acuity of anisometropic amblyopia. Presence of eccentric fixation caused less improvement of visual acuity. Out of 50 children, 48 had central fixation and 2 had eccentric fixation with poor compliance. Forty-eight (96%) of the children had good compliance of amblyopic treatment whereas 2 (4%) had poor compliance. Among the 48 children with good compliance had improvement but can't get normal range because of the limitation of follow up. The improvement of visual acuity in children with poor compliance was slower than the children with good compliance. (Figure -09)

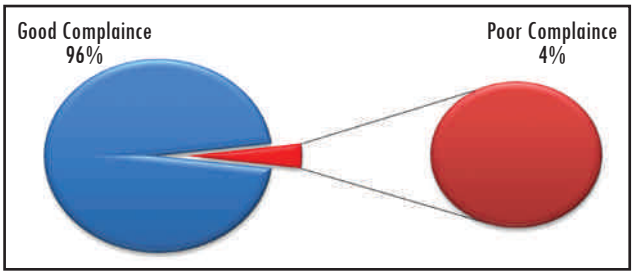
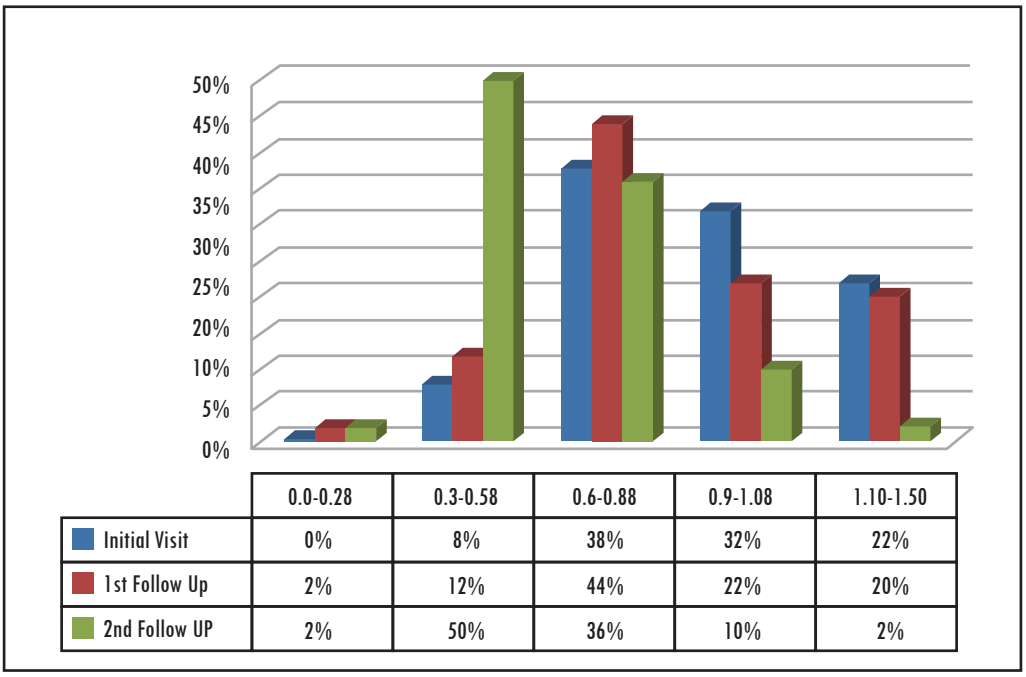


Figure - 09: Percentage of compliance among the subjects

Contrast Sensitivity Function

The difference of contrast sensitivity between amblyopic eye and better eye became progressively greater as the depth of anisometropic amblyopia increase. There was a strong relationship between depth of amblyopia and contrast sensitivity. A quantative assessment showed that there was also a significant correlation between the degree of Anisometropia and the contrast sensitivity between the eyes significant with Pearson correlation. Mean initial aided contrast sensitivity 0.89 ± 0.25 log MAR in amblyopic eye and aided contrast sensitivity in better eye 0.44 ± 0.25 log MAR unit (Figure 10 & 11). Mean contrast sensitivity was improved after occlusion therapy 0.27± 0.26 in the amblyopic eye and in batter eye 0.05 ± 0.9 log MAR.



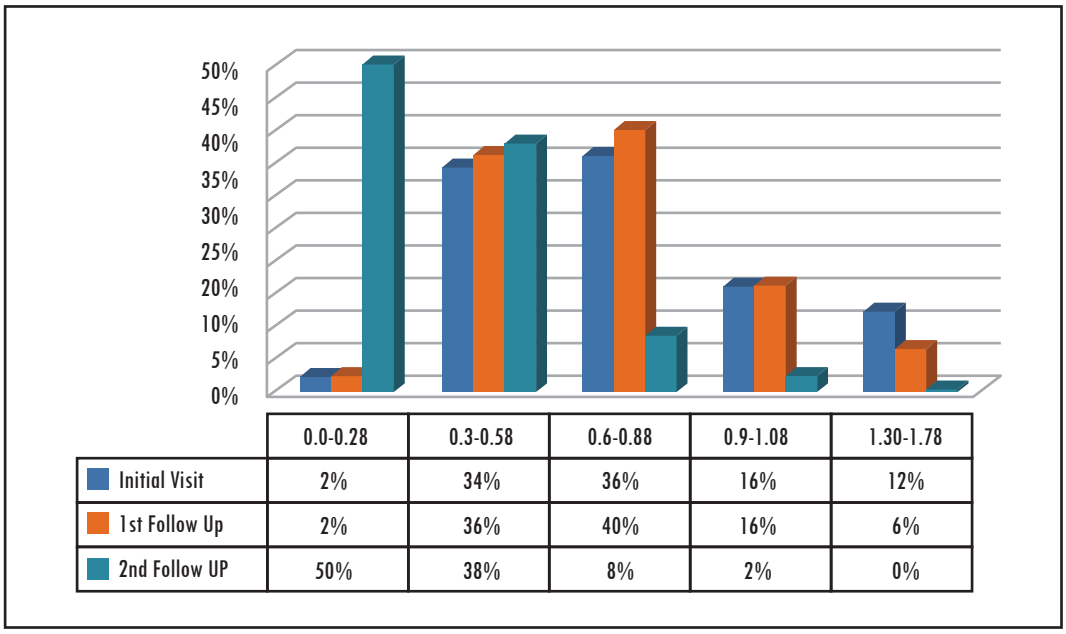
	0.0-0.28	0.3-0.58	0.6-0.88	0.9-1.08	1.10-1.50
Initial Visit	0%	8%	38%	32%	22%
1st Follow Up	2%	12%	44%	22%	20%
2nd Follow UP	2%	50%	36%	10%	2%

Figure - 10: Percentage of compliance among the subjects

Outcome of Anisometropic Amblyopia:

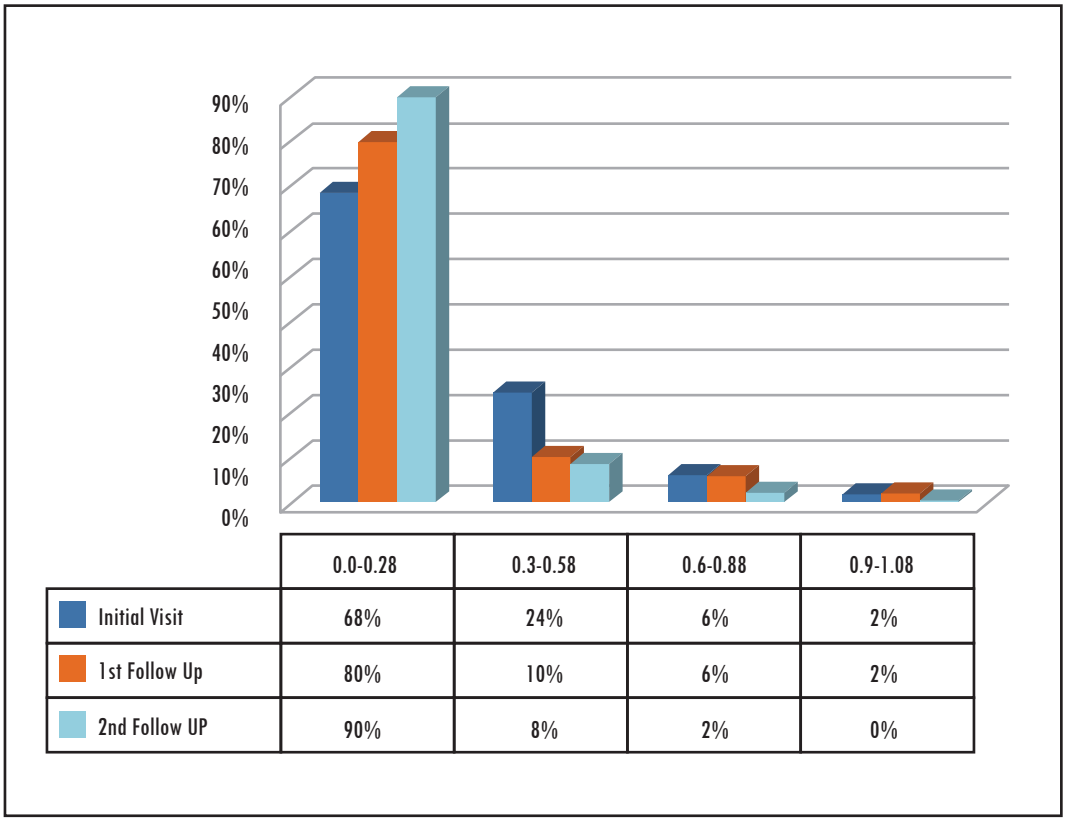
Improvement of Visual Acuity

In Figure 11 & 12, the mean baseline visual acuity of the amblyopic eye prior to starting occlusion therapy was 0.67 ± 0.32 log MAR unit which improved to 0.33 ± 0.26 LogMAR units. At the 3 months of outcome visit amblyopic eyes improve average >2 lines. Initial visual acuity in the better eye improved 0.16 ± 0.24 log MAR unit to 0.06 ± 0.14 LogMAR units. Among 50 children, 29 (58%) given full time occlusion of 8 hours, 21 (42%) given part time occlusion of 6 hours. Best corrected visual acuity at the initial visit was 0 (0%) of 0.0 to 0.2 LogMAR, 17 (34%) of 0.22 to 0.5 log MAR, 19 (38%) of 0.52 to 0.8 logMAR, 8 (16%) of 0.82 to 1.08 LogMAR and 7 (14%) of 1.3 to 1.80 LogMAR unit. After occlusion therapy of three month, 23 (46%) of 0.0 to 0.2 log MAR, 20 (40%) 0f 0.22 to 0.5 log MAR, 5 (10%) 0f 0.52 to 0.8 LogMAR, 1 (2%) of 0.82 to 1.08 log MAR and 1 (2%) of 1.3 to 1.8 log MAR. Two children are not improving because of less use of occlusion therapy. Binocular vision improves by 80% at the time of completion the treatment. Pearson correlation confirmed significant visual outcome difference before and after treatment (x^2= 0.65; $p<0.05$).



	0.0-0.28	0.3-0.58	0.6-0.88	0.9-1.08	1.30-1.78
Initial Visit	2%	34%	36%	16%	12%
1st Follow Up	2%	36%	40%	16%	6%
2nd Follow UP	50%	38%	8%	2%	0%

Figure- 11: Percentage of compliance among the subjects



	0.0-0.28	0.3-0.58	0.6-0.88	0.9-1.08
Initial Visit	68%	24%	6%	2%
1st Follow Up	80%	10%	6%	2%
2nd Follow UP	90%	8%	2%	0%

Figure- 12: Percentage of compliance among the subjects

Discussion

Anisometropic amblyopia is a common cause of amblyopia that has an estimated prevalence in the pediatric population ranging from 2% to 5%. The prevalence of various magnitudes of anisometropia remains relatively constant with age. Children less than 8 years of age were much less likely to had amblyopia than older children[1].The mean age was 10.02 years. While after age of 8 years, the prevalence of amblyopia did not change substantially but the severity did. Nearly 80% of anisometropic children under age 8 years had either mild or moderate amblyopia[2]. In our study about 10% children had mild amblyopia, 26% had severe amblyopia and 64% had moderate amblyopia. This finding supported by another study where they reported that older children were at a great risk for severe amblyopia[11]. This provides support for screening to detect children at risk for amblyopia prior to age 6-8 years, as amblyopia density appears to increase in older children.

Hyperopic anisometropia was more common than myopia in this study. Astigmatism >1.50 D was major cause of development of amblyopia. This finding is consistent with the finding of previous study which found that 95% of the subjects with amblyopia were found to have astigmatism[3]. If amount of refractive error is high in the amblyopic eye, risk of developing severe amblyopia increase. In this study also demonstrated a strong relationship between the magnitude of anisometropia and the depth of amblyopia. Mild anisometropia produces only a minimal visual defect. Over 36% of children having >2 D of anisometropia presented with mild or moderate amblyopia (two lines of acuity difference or less). In contrast, over 38% of children >4 D of anisometropia had moderate or severe amblyopia. According to previous study reported that over 80% of children having <2D of anisometropia had no amblyopia or only mild amblyopia and 60% of children with >4D of anisometropia had moderate or severe amblyopia[14].

Present results of the study also demonstrated that larger degree of anisometropia can generally induce poor fusion and subnormal stereopsis[11]. When anisometropia magnitude (AM)<3.0D, about 93% patients have fusion function with worth 4 dot test, and 80% patients retain stereopsis (smaller than 1200 sec arc) with Lang stereo acuity test. When 3.0D<AM<6.0D, about 50% patients retain fusion, about 80% patients had absence of stereopsis function (larger than 1200 sec arc). At last, when AM>6.0D, about 83% of the patients had absence of fusion (active suppression), and almost 91.67% had lost the function of stereopsis (larger than 1200 sec arc). Previous study also demonstrated that binocular functions are relatively developed normal in low anisometropes (AM<3.0D), but when AM>3.0D, especially for the anisometropes whose AM is larger than 6.0D, fusion and stereopsis function are seriously influenced[12]. The suppression and stereopsis function will change significantly as the degree of anisometropia varies. Occlusion or pharmacological penalization of the sound eye remains the most accepted treatments for amblyopia. About 75% of patients improve with treatment[5]. Occlusion of the non-amblyopic eye has been the major therapy of amblyopia. Though full-time occlusion has been classically used as an effective method, there is no proven advantage of longer daily occlusion hours. Opinions vary on the number of daily occlusion hours, and there have not been conclusions about the most effective and optimal regimen[8]. Other study reported that solitary 6-hour occlusion therapy revealed an effective improvement of the best-corrected visual acuity and provided good maintenance of improvement in the treatment for monocular amblyopes aged 3 to 8 years[10]. Young et al (2006) reported that the efficiency of amblyopia treatment was substantially poorer in children older than 8 to 12 years, and that this efficiency decreased as a function of age[2].

The lower treatment efficiency in older children might be related to their poor compliance[6]. We did counseling to our patient's parents to cover their children's sound eye outside of school hours and to observe their children during the occlusion time. They also advised to observe supervise children daily activities such as watching TV, reading or computer operating for at least one hour during the occlusion time. In our study, 96% had good compliance and 4% had poor compliance. Such detailed instructions gave the parents a realistic opportunity to adhere to the treatment. The success rate in this study was 90% based on the post-treatment BCVA of LogMAR 0.1 or better. Earlier studies also reported that the final vision in 94% of the patients improved by at least two lines after full-time occlusion therapy. Improvement in visual acuity usually occurred within 3 months.

Previous study reported that during the first quarter (0-3 months) of the amblyopia treatment there were 3.6 lines of improvement for the oldest group and 4.1 lines for the youngest group, while relatively minor improvements were obtained at later dates. Our study is completely matched with him[11].

Others study also reported that the duration required to achieve a stable vision improvement had been 5.77, 6.31, 5.27 and 5.22 months in patients aged 11 to 13 and 14 to 15 years, respectively, while Park et al. found that the average treatment duration had been 10 months (range of 3-27 months), and improvement in visual acuity had mostly occurred in the initial 3-6 months of treatment. However, it appeared that the patients with the worst pre-treatment BCVA scores needed a longer period of occlusion therapy (p=0.019). Visual improvement which was calculated by subtracting the post-treatment LogMAR BCVA from the pre-treatment LogMAR BCVA, and occlusion time showed a positive function of correlation. Though it is not statistically significant occlusion time and pre-treatment LogMAR BCVA showed a weakly positive function[13].

The mean and standard deviation of present average CS was 0.89 ± 0.25 LogMAR and after intervention of amblyopia therapy with vision therapy mean and standard deviation of VA was 0.58 ± 0.26 LogMAR in amblyopic eye. In sound eye initial contrast sensitivity was 0.44 ± 0.25 LogMAR and after therapy contrast sensitivity was 0.35±0.9 LogMAR. After occlusion therapy not only improves the VA but also improve the contrast sensitivity.

Conclusion

Children with anisometropic refractive error are less likely to have amblyopia if they detected at a young age. It is expected that the occlusion therapy along with active vision therapy outside of school hours can be effectively used in anisometropic amblyopia. Success rate of anisometropia treatment depends upon the co-operation of child and parents. Thus, present study demonstrated that depth of amblyopia increased with higher degree of anisometropia. This study concludes that, earlier diagnosis and treatment of anisometropic amblyopia lead to better improvement.

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