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ARTICLE

CLINICAL CHARACTERISTICS OF CHILDREN WITH REFRACTIVE AMBLYOPIA AT CIPTO MANGUNKUSUMO NATIONAL REFERRAL HOSPITAL

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ABSTRACT

Amblyopia, commonly referred to as 'lazy eye', manifests as a reduction in best corrected visual acuity (BCVA) in the absence of detectable ocular structural abnormalities. Refractive amblyopia specifically denotes a subtype of amblyopia arising from uncorrected refractive errors. We conducted a retrospective descriptive analysis on the medical records of all children diagnosed with refractive amblyopia at the Department of Ophthalmology, Cipto Mangunkusumo Kirana National Referral Hospital, Jakarta, Indonesia in 2018 to 2022. After which, 391 eyes of 224 patients with refractive amblyopia were considered eligible for inclusion. Median age was 8 (5-18) years, with the majority of patients being older than seven years of age (58.7%). Leading method of treatment was with spectacles alone (80.4%). Overall amblyopia improvement was mostly observed after six months of treatment. In conclusion, refractive amblyopia at our hospital was highly prevalent among children. Therefore, timely detection and management of refractive errors in children is essential in the prevention of refractive amblyopia.

Keywords: Amblyopia; Children; Refraction; Spectacles

АБСТРАКТ

Амблиопия, обычно называемая "ленивым глазом", проявляется в виде снижения остроты зрения с наилучшей коррекцией (BCVA) при отсутствии выявляемых структурных аномалий глазного дна. Рефракционная амблиопия обозначает подтип амблиопии, возникающей из-за некорригированных аномалий рефракции. Мы провели ретроспективный описательный анализ медицинских карт всех детей с диагнозом "рефракционная амблиопия" в отделении офтальмологии Национальной специализированной больницы Cipto Mangunkusumo Kirana, Джакарта, Индонезия, в период с 2018 по 2022 год. После этого 391 глаз 224 пациентов с рефракционной амблиопией был признан пригодным для включения в исследование. Средний возраст составил 8 (5-18) лет, большинство пациентов были старше семи лет (58,7 %). Ведущим методом лечения были только очки (80,4 %). Общее улучшение состояния амблиопии наблюдалось в основном после шести месяцев лечения. В заключение следует отметить, что рефракционная амблиопия в нашей больнице была очень распространена среди детей. Поэтому своевременное выявление и лечение аномалий рефракции у детей имеет большое значение для профилактики рефракционной амблиопии.

Ключевые слова: Амблиопия; дети; рефракция; очки

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INTRODUCTION

Amblyopia is characterized by a decrease in best corrected visual acuity (BCVA) in the absence of anatomical anomalies of the eye. Amblyopia is related to disruptions in the visual experience that may be attributed to refractive errors that occur during critical periods of development in early life.[1] Refractive errors account for the cause of 60-80% of visual impairment in children. Moreover, previous studies reported that 2-11% of children under the age of 16 years have refractive errors.[2,3] Prompt detection and treatment is essential as uncorrected refractive error during a child's critical period of visual development could lead to amblyopia.[4]

Diagnostic criteria for amblyopia is a BCVA of less than or equal to 6/12 with the presence of amblyogenic factors, and is considered unilateral when there is more than a difference of 2 lines between the eyes. Amblyopia can be bilateral or unilateral, although the latter is generally more common.[1,5]

Estimated global prevalence of amblyopia is 1.36%.[6] Meanwhile, a prior study conducted in Jakarta, Indonesia by Anggraini *et al.* reported a slightly higher prevalence of 2.7% among school-aged children, in which all of the patients with amblyopia were caused by refractive error.[7] Moreover, other studies in India and Singapore also found refractive amblyopia to be the most common type of amblyopia.[8, 9] Refractive amblyopia is majorly caused by anisometropia, where the differing refractive status of each eye causes constant retinal defocus. Isometropia may also cause amblyopia, whereby amblyopia occurs due to high bilateral refractive error that is left uncorrected.[10]

In Asian countries, myopia and astigmatism were often found to be the most common refractive error among school children; a study in Singapore reported 11% with myopia and 8.3% with astigmatism[11], while in Bhutan astigmatism was higher with 9.75% and myopia at 6.64%.[12] A multi-ethnic study on school children conducted in United Kingdom reported that children of South Asian ethnicities had the highest rates of myopia (25.2%) in comparison to other ethnicities, and also had longer axial lengths.[13]

Mainstay therapy of refractive amblyopia includes spectacles and occlusion therapy. Prompt therapy of amblyopia is associated with more favorable outcomes. Visual acuity improvement is often observed within 10 to 45 weeks of treatment.[1]

Prompt detection and proper management of refractive errors and amblyopia in childhood is crucial for preventing vision loss and ensuring proper growth and development. A prior study reported that children with amblyopia demonstrated comparatively worse higher-order visual processing skills than their peers with normal vision, and amblyopic children tend to have weaker visual search and attention, especially when faced with greater demands of executive function[14], and another study reported that children with residual amblyopia demonstrated poorer eye-related quality of life and functional vision than their peers.[15]

Proper development of motor skills during childhood hinges on the preservation of proper binocular vision. However, exposure to inappropriate visual input due to amblyopia can impede this process. Thus, these developmental shortcomings may impede learning essential skills such as reading, a complicated skill that needs proper cognitive, sensory, and ocular motor competencies which may be difficult with amblyopia; with a prior study showing slower reading among children with amblyopia.[16] Thus, preventing amblyopia is important to ensure proper visual development that can have further implications to a child's education and quality of life in their future. As one of the main causes of amblyopia is uncorrected refractive error, early screening prior to starting school is essential to promptly detect any present refractive error and ensure timely treatment. It is important to recognize potential amblyogenic factors that may be present in these children as well as to ensure proper early detection for amblyopia.[10] Early detection is important as it is agreed upon that initiating

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treatment of amblyopia before seven years of age is more effective, and thus allows for lesser risk of vision loss.[4]

With early diagnosis and treatment of refractive errors being key in prevention and treatment of amblyopia, our study thus aims to describe the demographic and clinical characteristics of all pediatric patients with refractive amblyopia at our hospital, as well as to evaluate their associated amblyogenic factors and outcome of therapy.

MATERIAL AND METHODS

A descriptive analysis was conducted retrospectively on the medical records of all children diagnosed with refractive amblyopia at the Department of Ophthalmology, Cipto Mangunkusumo Kirana National Referral Hospital, Jakarta, Indonesia within 2018 to 2022. This study was conducted while adhering to the Declaration of Helsinki and was given ethical clearance and approval by the Health Research Ethics Committee of University of Indonesia-Cipto Mangunkusumo Hospital (HREC-FMUI/CMH). We excluded patients whose records were not complete or were inaccessible. Obtained data included demographic data (age at diagnosis, gender, laterality), classification of refractive amblyopia (anisometropia or isometropia), degree of amblyopia, amblyogenic factors, type of therapy given, as well as uncorrected visual acuity (UCVA) at first visit, and best corrected visual acuity (BCVA) after correction. Follow-up data was extracted at three months, six months, and one year after therapy. Isoametropic amblyopia was defined as amblyopia that occurs in both eyes due to relatively similar bilateral refractive error, while the definition of anisometropic amblyopia was amblyopia that occurred because of spherical equivalent difference of > 3D between both eyes. Amblyogenic factors were defined as risk factors that can lead to amblyopia, with amblyogenic factors of isoametropic amblyopia are myopia > -5.00 D, hypermetropia > +4.00 D and astigmatism > 2.00 D; amblyogenic factors of anisometropia amblyopia include anisomyopia > -3.00 D, anisohyperopia > +1.50 D, and anisoastigmatism > 2.00 D.

This study conducted a descriptive analysis on the included patients' data. Quantitative variables were presented based on data normality according to the Kolmogorov-Smirnov test as mean (standard deviation) or median (minimum-maximum), while categorical variables were depicted in frequency and percentage. For quantitative analysis of visual acuity, visual acuity was converted to logMAR (logMAR of 0.0 was equivalent to 6/6 or decimal of 1.0). Therapeutic efficacy was defined as visual acuity improvement during follow-up. Data input and analysis was done with Microsoft Office Excel version 16.48 and IBM SPSS (Statistical Package for the Social Sciences) version 26.

RESULT

In this study, 391 eyes of 224 patients were included, and Table 1 presents the summary of baseline characteristics of the included patients.

Average age at diagnosis of included patients was 8 (3-18) years, with majority of the patients being older than 7 years of age (60.3%). This highlights that at our hospital, the average age of amblyopia detection (and therefore initiation treatment) at our hospital has a relatively wide age range in which the children tend to be relatively older and in the school-going age. Females constituted over half (55.4%) of the study population.

Table 1. Baseline characteristics of included patients, n = 224

Characteristic	n (%)
Gender	
Male	100 (44.6)
Female	124 (55.4)
Age (years)	
≤ 7 years	89 (39.7)
> 7 years	135 (60.3)

Clinical characteristics of patients with refractive amblyopia was summarized in Table 3. Anisometropic amblyopia was the most prevalent type of amblyopia (52.4%), and

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most eyes (67.5%) had mild-moderate degree of amblyopia, which was defined as BCVA of 6/12 to 6/24. The most common amblyogenic factor was myopia, followed by astigmatism and hyperopia.

Table 2. Clinical characteristics of patients with refractive amblyopia, n = 224

Characteristic	n (%)
Amblyopic status	
Isometropia	72 (24.8)
Anisometropia	152 (52.4)
Laterality	
Unilateral	57 (25.4)
Bilateral	167 (74.6)
Degree of amblyopia	
OD, n = 200	
Mild-moderate	135 (67.5)
Severe	65 (32.5)
OS, n = 191	
Mild-moderate	129 (67.5)
Severe	62 (32.5)
Amblyogenic factor	
OD, n = 200	
Myopia	126 (63)
Astigmatism	63 (31.5)
Hypermetropia	11 (5.5)
OS, n = 191	
Myopia	123 (64.4)
Astigmatism	56 (29.3)
Hypermetropia	12 (6.3)

OD: Ocula dextra; OS: Ocula sinistra

Prescribed amblyopia therapy was summarized in Table 3. The most prescribed treatment was spectacles (80.4%), followed by spectacles with occlusion therapy (19.2%).

Table 3. Amblyopia therapy, n = 224

Therapy	n (%)
Spectacles	180 (80.4)
Spectacles + occlusion therapy	44 (19.6)

Analysis of visual acuity following therapy was done in 53 patients at 3-month, 6-month, and 1-year follow-up, as shown in Table 4. Median initial UCVA was 1.48 (0-2.8) logMAR, which improved to a BCVA of 0.56 (0.1-1.78) logMAR after correction at first visit. At 3-month follow-up, further improvement in BCVA was observed with an average of 0.46 (0-2.08) logMAR, and this trend of improvement was again observed at the 6-month mark with an average BCVA of 0.44 (0-1.32) logMAR. This improvement was again observed at 1-year follow-up with an average BCVA of 0.51 (0-1.78) logMAR, however, only 21 subjects had available data at last follow-up. Statistical analysis using the Friedman non-parametric test revealed that overall improvement of visual acuity from baseline was statistically significant ($p < 0.001$). Post-hoc Wilcoxon analysis showed that improvement from baseline to each follow-up was also statistically significant ($p < 0.05$).

Table 4. Visual acuity before after therapy,n = 391

	VA (logMAR)
UCVA	1.48 (0.8–2.08)
BCVA	0.56 (0.18–1.30)
Follow-up (BCVA)	
3 months, n = 90	0.46 (0.00–2.08)
6 months, n = 53	0.44 (0.00–1.32)
12 months, n = 35	0.51 (0.00–1.78)

UCVA: Uncorrected visual acuity; BCVA: Best corrected visual acuity

In terms of the proportion of patients that experienced improvement, it was observed that at 3-month follow-up, most eyes had not experienced improvement of visual acuity, with 52/90 (57.7%) with no improvement. However, at 6-month follow-up, majority (37/53, 69.8%) did experience visual acuity improvement, and this trend continued at 1-year follow-up (20/35, 57.1%). It is notable, however, that a large portion of patients were lost to follow-up, with data of only 35 eyes that was available at 1-year follow-up.

Refractive amblyopia is reported to be the most common type of amblyopia among children,[6, 8, 17] ranging from 45.29% in India[8] to 84% in Singapore[9]. Our study revealed that in the years 2018 to 2022, 391 eyes of 224 patients presented to our clinic with refractive amblyopia. This particularly high rate may reflect the lack of awareness regarding eye

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health screening in school aged children among the general public in Indonesia; in which late detection of refractive errors can result in further visual disorders and refractive amblyopia.[8]

DISCUSSION

The average age at diagnosis of refractive amblyopia in our study was 8 years, with a very wide range spanning from as young as 3 years old to as old as 18 years old. Furthermore, more than half of our patients were more than 7 years of age; therefore, it is evident that the average age at which refractive amblyopia is diagnosed (and subsequently treated) in our hospital encompasses a broad age range, with children typically being older and of school-age. This is comparable to findings by Mocanu et al.[18] and Aljohani et al.[19] which report the average age of amblyopia in their cohorts to be 9.94 ± 2.75 years and 8.93 ± 3.67 years, respectively. Amblyopia occurs due to impaired visual stimulation during the crucial age of visual function development; vision deprivation as a result of refractive errors leads to disturbances in the visual system's ocular, synaptic and cortical maturation in this critical time period, thus leading to amblyopia. Detection of refractive errors should be carried out in children in their pre-school era (3-4 years of age), as early detection in this period is considered effective in reducing the risk of amblyopia.[20,21] Given the considerably high prevalence of refractive amblyopia observed in our study, alongside the fact that they are relatively older and are of school-going age, this emphasizes the importance of early detection and intervention of refractive errors (as a significant amblyogenic factor) in pre-school aged children as a means to potentially reduce the prevalence of preventable refractive amblyopia in the future population.

Our study reported a higher percentage of males to females, with a ratio of 1.3:1. Previous studies have described that refractive amblyopia has no predilections in terms of gender as a risk factor.[22]

Most amblyopic patients had bilateral presentation in our study, and this is in line with previous studies which report that 59%[8] and 87.5%[23] of their amblyopic patients also presented bilaterally. On the other hand, a study in Singapore reported their cohort of mostly unilateral amblyopia accounting for 61% of their study group.[9]

The most prevalent amblyogenic factor in this study was myopia followed by astigmatism. This is in line with the global prevalence meta-analysis study by Hashemi et al.,[3] which stated that myopia and astigmatism are much higher in Asian countries. In a study from Singapore, myopia prevalence was reported at 11.0%, followed by astigmatism (8.3%), while hypermetropia was only 1.4%.[11] Similarly in Bhutan, the prevalence of astigmatism was 9.75%, myopia was 6.64% while hypermetropia was 2.17%.[12] In a multi-ethnic study by Rudnicka et al., myopia was highest among those of South Asian ethnicity at 25.2%, while Africans were 10%, and Europeans were 3.4%.[13] Moreover, the study reported that axial length of those with Asian ethnicity was longer, despite anterior chamber depth and surface keratometry being the same among other ethnicities. Apart from this, greater occurrence of myopia in Asia is also influenced by genetic factors. Supporting this theory, previous studies by Masters et al. stated the incidence of myopia in Asia was associated with a flatter face shape, larger eye size in a smaller orbital cavity which can trigger the eyeball to elongate axially.[24] In addition, an external factors such as lack of outdoor activities is prevalent in Asian educational systems.[25-27] Therefore, the relatively high rates of myopia in Asian countries underscore the crucial role of screening for refractive errors and potential amblyogenic factors in young children. This highlights the importance of both the public health approach in increasing awareness for the implications of improper refractive error treatment, screening and early treatment of refractive errors in primary healthcare centers, as well as timely referral to tertiary centers when necessary, as to mitigate the global burden of visually impaired children as

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a result of amblyopia and their associated underdeveloped visual function.[4]

Refractive amblyopia encompasses both anisometropic and isoametropic amblyopia. In our study cohort, most of the patients had anisometropic amblyopia. Saeed et al. also found anisometropia to be the most predominant cause (80.56%) of pediatric unilateral amblyopia.[19] Similar results were found in studies by Bamhane et al.[28] and Janti et al.[29] where the percentage of anisometropic amblyopia was higher (53.3% and 36.2%). Moreover, children are generally unaware of unilateral refractive errors as visual function is typically compensated by the non-amblyopic eye.[28]

In our study, mild-moderate amblyopia accounted for the most common severity of amblyopia. This is comparable to Jarwal et al's study which reported 64% of their cohort had mild-moderate amblyopia and 36% had severe amblyopia.[30]

The principle of management of refractive amblyopia is refractive correction and optimizing amblyopic vision, which is traditionally achieved via occlusion of the non-amblyopic eye. All modes of treatment in this study incorporated refractive correction using spectacles, with the majority (80.4%) using only spectacles, followed by 19.6% that also incorporated occlusion therapy. Previous studies found that refractive amblyopia therapy with glasses alone for 16-18 weeks can improve visual acuity up to 3 chart lines in unilateral refractive amblyopia patients, and 4 chart lines in bilateral amblyopia. While isoametropic amblyopia can be treated with refractive correction alone, anisometric amblyopia requires both spectacles and occlusion therapy.[1,31]

In addition to refractive correction, occlusion therapy is needed in treating anisometropic amblyopia.[1,32] Based on The Amblyopia Treatment Studies, moderate amblyopia can benefit from occlusion of the non-amblyopic eye for 2 hours each day, and severe amblyopia can benefit from 6 hours each day, such recommended dosing can improve visual acuity.[4] Response to therapy is often most effective before 12 years of age, with declining response as children get older.[28] Buckle et al. study described the success of refractive correction therapy for 12-14 weeks along with 17 weeks of occlusion therapy in patients with severe amblyopia, with 67% of patients experienced an improvement in visual acuity up to 0.4 logMAR.[32] In our study, there was improvement from baseline average UCVA to BCVA, and this improvement continued at each follow-up. Although it is notable that this improvement was not optimal due to their amblyopia and thus could not reach 6/6 (or 0.0 logMAR); this improvement, although not optimal, is still important in improving the visual acuity of children with refractive amblyopia. The age at which refractive amblyopia was diagnosed and therapy was initiated in our patient population was on average 8 (3-18) years of age, with this broad age range, we can infer that some of our patients did not start amblyopia therapy at the ideal age (before 12 years of age).[28] This highlights the importance of early detection of refractive amblyopia, which can then allow for the initiation of treatment to be as early as possible to optimize a child's visual function to best facilitate their learning process and development for school and their future.

In our study, only 35 of 391 eyes had follow-up data available after one year, where the majority of our patients did not return for their follow-up evaluation. Subjects that were lost to follow-up were on average 9 years of age, with the youngest being 6 years old. As these children are of school age, their loss to follow-up may be explained by their school schedule coinciding with the outpatient clinic schedule, as well as the potential lack of awareness from their caregivers regarding the importance of returning for follow-up.

In terms of average visual acuity improvement, our study reported a statistically significant improvement from baseline at each follow-up. Meanwhile in terms of proportion of patients with improvement of visual acuity, improvement was observed in most patients starting at the 6-month follow-up. Buckle et al.'s study had similar results to

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this study; at 32 weeks after therapy, 71% of moderate amblyopia patients had an improvement in BCVA of around 0.3 logMAR, however no additional progress was seen after 48 weeks. On the other hand, among those with severe amblyopia, a higher proportion (55%) was seen with improved BCVA of approximately 0.4 logMAR after 48 weeks, in comparison to at 32 weeks (40%), although further follow-up also showed no additional changes.[32] Papageorgiu et al. also explained that improvements in visual acuity in amblyopia patients began to be seen at 4-12 weeks until 30 weeks later they entered a plateau phase or only slight improvements occurred. The success of refractive amblyopia therapy can be influenced by various factors, including age at diagnosis of amblyopia, age at initiation of therapy, type of amblyopia, initial visual acuity, duration of amblyopia, type of therapy and level of patient adherence to therapy.[33]

Limitations of this study include the lack proper follow-up, in which less than ten percent of the total number of patients were compliant with follow-up. While this is a retrospective study and thus serves as an accurate portrayal of our study population's lack of compliance towards follow-up, this limits this study's ability to properly evaluate the treatment outcomes of most of these patients. Loss-to-follow-up can potentially be caused be by lack of understanding from the patient's parents or caregivers regarding the importance of routine evaluation of refractive errors and amblyopia. Therefore, disease education is important so that the outcome of therapy can be better monitored in the future.

CONCLUSION

Refractive amblyopia at our hospital was highly prevalent among children who present with refractive errors. The most common amblyogenic factor was myopia. The preferred mode of amblyopia therapy was refractive correction alone, with visual acuity improvement observed mostly after six months of treatment. Further studies with a more robust follow-up schedule is needed.

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DECLARATIONS

Author contribution. Conceptualization and research design: DEY, JDB, RSS, MRP; Data collection and curation: DEY, JDB, RSS, MRP, DAS;Data analysis and interpretation: DEY, MRP, DAS; Critical revision and review of the manuscript was performed by DEY, JDB, RSS, MRP, DAS. The authors read and approved the final manuscript.

Conflict of interest. The authors declare no conflict of interest. This research did not receive any financial support from any research grant.

Additional information. This study was granted ethical approval by the Health Research Ethics Committee of University of Indonesia-Cipto Mangunkusumo Hospital (HREC-FMUI/CMH), No: KET-279/UN2.F1/ETIK/PPM.00.02/2023, and was conducted in accordance with the Declaration of Helsinki.

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