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Risk factor of amblyopia in children in Madagascar

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Abstract

Purpose: The aims of this study was to determine risk factor of amblyopia in malagasy children.

Methods: It was a case-control study doing at Hospital University Joseph Ravoahangy Andrianavalona from 1st september to 01st february 2022. The case were children who had functional amblyopia. The control were children who didn't have amblyopia and came to the hospital for vision anomaly and had a similar demography specificity like case. The number of controls was twice the number of cases. All children with organic ophthalmic pathologies were excluded. The data was processed by Epi.info 7.0 software. We used Odds Ratio (OR) test to find association between amblyopia and risk factor. Confidence interval (CI) was fixed at 95%. Association was significant for a value of $p < 0,05$.

Results: 38 cases was found for 76 controls. A significant association was found for amblyopia and personal history OR:4,85CI[1,87-12,58] $p < 0,00$; familial history OR :4,84CI[2,02-11,59] $p < 0,00$; for esotropia OR :6,60CI[2,62-16,56] $p < 0,00$; for exotropia OR :3,07CI[1,21-7,75] $p < 0,01$; for anisometropia OR :26,90CI[5,73-126,16] $p < 0,00$; for hyperopia OR:4,16CI[1,69-10,25] $p < 0,0$ and for astigmatism OR :0,22CI[0,08-0,57] $p < 0,00$.

Conclusion: Functional amblyopia was associated in children with personal and family history of strabismus and ametropia. Children with esotropia, exotropia, hyperopia, astigmatism, and anisometropia was associated with functional amblyopia. A systematic vision field is necessary for patient with risk factor.

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Introduction

Amblyopia, the leading cause of visual impairment in children, is defined as unilateral or bilateral visual loss with no ocular pathology [1]. There are two types: functional amblyopia and organic amblyopia. However, the majority of amblyopia observed in current practice are unilateral and functional. It is associated with refractive error, strabismus, or anisometropia [2] [3] [4]. Its screening was necessary because it can cause irreversible visual loss, justifying an ophthalmological examination in all children before the age of 3 or 4 years [5-6]. Early childhood vision screening was recommended for detecting preventable and treatable vision disorders [1-3]. Early diagnosis and appropriate treatment of strabismus in a child can restore better visual acuity and binocular single vision, reduce the development of amblyopia and subsequent occurrence of misalignment, maximize visual potential and prevent possible visual impairment, and potentially sustain long-term visual quality [5-7]. In developing country like Madagascar, accessibility of health care service is more difficult. Knowledge of risky situations improve detection of amblyopic children. The purpose of this study was to identify

associated factors with functional amblyopia in children in Madagascar.

Method

A case-control study was carried out at University Center Joseph Ravoahangy Andrianavalona Hospital of Antananarivo from 01st September 2020 to 01st February 2022. The cases were all children who had a functional amblyopia during this period. The controls were all children who had eye examination during this period, the same demographic profiles as the cases, and who did not have an amblyopia. The number of controls was twice the number of cases. All children with organic pathologies were excluded.

All children had completed ophthalmological examination. Each parent was asked for children's personal and family history. To identify strabismus, cover-uncover tests for near (33 cm) and distance (6 m) were performed. Constant strabismus was diagnosed if tropia was present at distance and near fixation; if it was not present, then it was defined as intermittent. Strabismus was classified by tropia primary direction as esotropia, exotropia. A refraction examination with

cycloplegia was used to detect refractive problems such as hyperopia, myopia, astigmatism and anisometropia. Anisometropia was defined as a difference in refraction between the 2 two eyes.

The data collected was processed by Epi.info 7.0. The Odds Ratio (OR) test was used to investigate the association between amblyopia and risk factors. The confidence interval (CI) was set at 95%. The association was significant for a value of $p < 0.05$.

Result

38 cases were observed for 76 controls. A significant association was found for amblyopia and personal history (OR, 4.85 ;95% CI, 1.87-12.58, $p < 0.00$) and family history (OR, 4.84 ; 95% CI, 2.02-11.59, $p < 0.00$); for esotropia (OR, 6.60 ;95%CI, 2.62-16.56, $p < 0.00$) and exotropia (OR, 3.07 ; 95%CI, 1.21-7.75, $p < 0.01$); for anisometropia (OR, 26.90 ; 95% CI, 5.73-126.16, $p < 0.00$) ; for hyperopia (OR, 4,16 ; 95% CI, 1.69-10.25, $p < 0,0$) and astigmatism (OR, 0.22 ; 95% CI, 0.08-0.57, $p < 0.00$). (Table 1).

Table 1. Ocular condition associated with amblyopia.

| Risk factor | Amblyopic children (%) n=38 | Non amblyopic children (%) n=76 | Odds Ratio (95% CI) | p |
|-------------------------|--------------------------------|------------------------------------|---------------------|-------|
| Personal history | | | | |
| Yes | 15 (39.47) | 9 (11.84) | 4.85(1.87-12.58) | <0.00 |
| No | 23 (60.52) | 67 (88.16) | | |
| Family history | | | | |
| Yes | 19 (50.00) | 13 (17.11) | 4.84(2.02-11.59) | <0.00 |
| No | 19 (50.00) | 63 (82.89) | | |
| Esotropia | | | | |
| Yes | 19 (50.00) | 10 (13.16) | 6.6(2.62-16.56) | <0.00 |
| No | 19 (50.00) | 66 (86.84) | | |
| Exotropia | | | | |
| Yes | 13 (34.21) | 11 (14.47) | 3.07(1.21-7.75) | <0.01 |
| No | 25 (65.79) | 65 (85.53) | | |

| | | | | |
|----------------------|------------|------------|--------------------|-------|
| Hyperopia | | | | |
| Yes | 30 (78.94) | 36 (47.36) | 4.16(1.69-10.25) | <0.00 |
| No | 08 (21.06) | 40 (52.64) | | |
| Astigmatism | | | | |
| Yes | 07 (18.42) | 38 (50.00) | 0.22(0.08-0.57) | <0.00 |
| No | 31 (81.58) | 38 (50.00) | | |
| Anisometropia | | | | |
| Yes | 16 (42.11) | 02 (02.63) | 26.90(5.73-126.16) | <0.00 |
| No | 22 (57.89) | 74 (97.37) | | |

Discussion

This study had some limitations. First, the study population comprised children who visited the Department of Ophthalmology care; this might be not representative compared with study doing in the community-based studies. Despite, this study can provided an important information of children’s risk of amblyopia in population and thus could conclusively demonstrate a relationship between amblyopia and potential risk factors. This study used a non-probability sampling method (i.e., a consecutive sampling approach) for the enrollment of study participants; therefore, it might have been influenced by the presence of outliers.

Personal history

A significant association was found for amblyopia and personal history (OR, 4.85 ; 95% CI, 1.87-12.58, $p < 0.00$). Getahun Agaje and al. found highly significant associations with neonatal factors, including gestational age ($P=0.01$), birth weight ($P=0.03$), and parent-reported admission to a neonatal intensive care unit ($P=0.01$). Children born at less than 37 weeks’ gestation had a 5-fold greater risk of having amblyopia (OR, 5.4; 95% CI, 2.3-12.3); 31% of children with amblyopia were born premature compared with 7.6% of children without amblyopia. Those with birth weights less than 2500 g were almost 5 times more likely to have amblyopia at the time of examination (OR, 4.8; 95% CI, 1.9-11.8). Admission to a neonatal intensive care unit was more commonly reported by parents of children with amblyopia (23.3%) than those of children without amblyopia (5.7%). The presence of this association also conferred a 5-fold increased risk of having

amblyopia (OR, 5.0; 95% CI, 2.1-12.0); this association remained highly significant ($P=0.01$) in the multivariate model [8]. It has been associated with assisted delivery (forceps or cesarean section), low birth weight and prematurity, neurodevelopmental disorders [9], refractive error [10], anisometropia, cranial nerve palsy [11], older maternal age at the time of childbirth [12], maternal cigarette smoking during pregnancy and a family history of strabismus [11].

Amblyopia was diagnosed in 31% of preterm births. In children born at less than 37 weeks of gestation, a 5-fold greater risk for amblyopia was identified (OR, 5.4; 95% CI, 2.3–12.3). A similar result was obtained for a birth weight less than 2500 g, where these children present a 5-fold greater risk for amblyopia (OR, 4.8; 95% CI, 1.9–11.8) [2]. The SPEDS identified a significant association between preterm birth [1]. A study from the United Kingdom, which included 293 prematurely born children, reported that low birth weight and gestational age are risk factors for amblyopia [13]. An Iranian study that included 164 children with refractive errors, 73 amblyopic children, and 91 non-amblyopic children, found that preterm birth presents a 7-fold greater risk for amblyopia (OR, 7.11; 95% CI, 2.28–22.14). Children with a low birth weight had a 6-fold greater risk for amblyopia (OR, 6.49; 95% CI, 2.29–18.32) [14].

Family history: refractive error, strabismus

A family history of amblyopia was another risk identified by our study (OR, 4.84 ; 95% CI, 2.02-11.59, $p<0.00$) which is consistent with medical literature. The ALSPAC (272 amblyopic/7825, 7 years old) reported that first degree relatives with amblyopia represent a risk factor in developing amblyopia [15]. Chia et al., in their Singaporean study, observed that in some sibling cases, both of the children were affected by amblyopia (2.3%) [16].

Sometimes, strabismus can lead amblyopia if there has neutralisation of one eye. That's why knowing family story of strabismus is important. The odds of being amblyopic among participants with a positive family history of strabismus were about 8 times (OR, 7.95, 95% CI: 2.09–30.22) more than those who had no positive family history [17]. Our study also agreed with a study done in Kosofe Town, Lagos state, Nigeria [18]. This can be explained by genetic factor. The importance of refraction and amblyopia, the evolution of strabismus following the different generations and shows that heredity gets an important part in the etiology of strabismus.

Esotropia

Esotropia was about (OR, 6.60 ; 95% CI, 2.62-16.56, $p<0.00$) more than those who had not esotropia. Similar result was found

by Mocanu V. et al. and had showed that the risk of being amblyopia was (OR, 10.39 ; 95% CI, 5.20–20.78, $p<0.001$) more than children who didn't have esotropia [19]. This common childhood oculomotor disorder results in manifested deviation with the absence of binocular vision [20]. In children, strabismus causes impaired depth perception and amblyopia [15, 21, 22, 23]. The study investigated 6-year-old amblyopic children identified esotropia in 11 of the 18 cases (61.1%) and exotropia in three of the 18 cases (16.7%) [2]. Similar proportions of exotropia and esotropia were obtained in the Friedman study which included white preschool children [4]. In the East Asian children study, esotropia was less prevalent than exotropia, probably due to the fact that the Asian population is more susceptible to myopia than to hyperopic refractive errors [24]. In contrast, an equal proportion of esotropia and exotropia was observed in East Asian children from the SPEDS [1]. In a Singapore study that included 1682 young children, exotropia in the amblyopic group was found in two cases and esotropia in one. The study found an association between amblyopia and strabismus (OR, 18.0 ; 95% CI, 3.3–97.8, $p = 0.001$) [16]. Other studies such as the Sydney Myopia Study (SMS) and the SPEDS also reported strabismus as a risk factor for amblyopia (OR, 13.1 ; 95% CI, 4.2–40.3 and OR, 65 ; 95% CI, 30–144) [1,2,23].

Exotropia

This study found an association between strabismus and amblyopia. The risk of being amblyopic was (OR, 3.07 ; 95% CI, 1.21-7.75, $p<0.01$) among children with exotropia more than children who didn't have strabismus. Other study find the same result and report that amblyopia was observed in children with exotropia in 3,38 times, 95% CI, 1.14-9.99, $p=0.0195$. This finding was statistically significant [20]. This can be explained by the fact that generally children had exotropia phoria and had a binocular vision, and had less amblyopia. That's way esotropia can caused amblyopia more than exotropia in our study.

Hyperopia

Hyperopia was the most prevalent refractive error in our examined population. Our study found an association between hyperopia and amblyopia OR, 4,16 ;95% CI, 1,69-10,25, $p<0,00$.

Children with hypemetropia had 4,16 times risk to have an amblyopia more than emmetrope children. In addition, having a hyperopia of ≥ 3.00 Ds was statistically significant with the development of strabismus (AOR=5.3). This was supported by other similar studies done in America [26], United Kingdom

[27], Australia [28], Nigeria [28], and Ethiopia [08]. Hyperopia of +3.00 Dioptria (D) and more is highly associated with the occurrence of esotropia and the odds of developing esotropic strabismus increases as the degree of hyperopia increases [29,30]. This research revealed that the odds of being amblyopic among participants having a refractive error of > +5D hypermetropia were about 22 times (OR, 21.77 ; 95% CI, 7.15–66.34) more than those participants who had no/mild refractive error [17]. This finding is consistent with a study done in China [31]. One explanation is that young subjects with hyperopia are usually asymptomatic because accommodation is very important in children, and thus hyperopia goes mostly undetected. The prevalence of amblyopia risk factors and the distribution of refractive errors in the pediatric population vary widely in the reported literature. This is attributed to the absence of unified cut-off limits used to diagnose the different refractive errors. Add to that the differences in ethnic backgrounds of the study populations, age groups and the instruments/ methodology used.

Astigmatism

Risk factor of being amblyopia was 0.22 ; 95% CI, 0.08-0.57, $p < 0.00$ for children with astigmatism. Prevalence in Northern Ireland (6–7 years 24.0%, 12–13 years 20.0%) and Ireland (6–7 years 19.2%, 12–13 years 15.9%) was high. Similar to other studies involving genetically isolated populations, it is significantly associated with persistent amblyopia in both cohorts [32,33].

The results from this current study suggest that astigmatism may be an important amblyogenic factor. However, the impact of cylindrical power on amblyopia might vary in children with either oblique or orthogonal astigmatism. Chou and colleagues found that the cylindrical power in children with oblique astigmatism was lower than that in children with orthogonal astigmatism. In previous electrophysiological studies, Yap et al. found that amblyopic children with high magnitude of astigmatism have diminished peak amplitudes in the orientation-specific visual evoked potentials in all the meridians tested, rather than in just a single meridian [34]. The relatively small sample size in our study did not permit us to investigate this in detail.

Anisometropia

The odds of being amblyopic was 26.9 ; 95% CI, 5.73-126.16, $p < 0.00$ among children with anisometropia. According to the literature, Anisometropia was found in 10 (28.6) of the amblyopic children and was associated with amblyopia [19]. A similar association was identified in the Singapore study (OR

20.6, 95% CI, 4.6–91.7, $p < 0.001$), the Sydney Paediatric Eye Disease Study (SPEDS) (OR 27.8, 95% CI, 11.2–69.3), the Sidney Myopia Study (OR 156 ; 95% CI, 64–382), and the Australian study (OR, 27.82; 95% CI, 11.17–69.31) [1,2,16,25]. In our study, the depth of amblyopia correlated with anisoastigmatism. Therefore, we might say that anisoastigmatism affected the depth of amblyopia. The impact of anisometropia on amblyopia was previously known, but further studies are needed on anisoastigmatism.

The odds of being amblyopic among participants who had anisometropia of greater than 2D were about 9.3 times (OR, 9.35 ; 95% CI, 2.86–30.60) more as compared to those who had no anisometropia [17]. In this study, the odds of being amblyopic among school age children who had anisometropia greater than 1D were about 10.44 times (OR, 10.44 ; 95% CI, 3.57–30.56) more than those who had no anisometropia. Refractive and strabismic amblyopia were not likely to be diagnosed the same way. Without a previous screening programme, 82% of refractive amblyopia were not followed at age 3–4 (and in all of those, parents said they did not intend to go to an ophthalmologist within the next year as they suspected nothing in their child), while most strabismic amblyopias were already under treatment. It seems that strabismic amblyopic children are sent to the ophthalmologist earlier, either because they develop signs perceived by paediatricians or primary care practitioners/parents, or because they belong to high risk groups, with earlier referral [35]. The amblyopia in children with anisometropia will be explain by unknowing the necessity of examination earlier before 1 year age. Generally, children don't know abnormal vision and don't develop sign before school age and number of parents ignore the necessity of eye screening.

Conclusion

This study shows that personal history, family history of strabismus or amblyopia and ametropia, strabismus, hypermetropia, astigmatism, anisometropia are factors associated with amblyopia. The ophthalmologist plays a great part for detecting of amblyopia in young children. Amblyopia is often hereditary, children presented risk factor most get regular examination to prevent him from amblyopia by a well directed treatment : accuracy of hidden hypermetropia, and treatment of "dominance". In dealing with child when the first sign of strabismus appears, he'll be able to secure to prevent him. Ophthalmologist may participate to inform pediatricians about the importance of a screening at an early stage, and he

also may participate at their practical formation for this first detecting.

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