

Prevalence and causes of childhood blindness in Huidong County, South China, primary ascertained by the key informants

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ABSTRACT

Purpose The aim of this study is to ascertain the prevalence and causes of childhood blindness and severe visual impairment (BL/SVI) in Huidong, South China.

Methods This cross-sectional study was conducted in early 2017 in areas of 139 816 children at the age of 0–15 as the study subjects. We used the trained key informants (KIs) to do preliminary visual test in the communities and refer those children suspected with blindness or unable to count fingers with both eyes at 5 m to hospital for further examination by paediatric ophthalmologist for causes. The WHO's definition of BL/SVI was used, as blindness is best-corrected visual acuity worse than 0.05 in better eye and SVI is equal to or better than 0.05 but worse than 0.1 in better eye.

Results Three hundred and fourteen KIs were trained. In total, 42 children with BL/SVI were found, and among them over half (22, 52.4%) were due to posterior segment disorders by anatomic site and 18 (42.9%) children were potentially preventable; these included BL/SVI caused by factors at children's development in intrauterine and after birth. This established the prevalence of BL/SVI was at 0.31/1000 (95% CI 0.28 to 0.34/1000).

Conclusion A low prevalence of childhood blindness was documented in this study. Establishment of surveillance system for disabled children including those with BL/SVI and better health education on eye care to the public according to the surveillance outcomes would help to reduce avoidable children's BL/SVI further in China.

INTRODUCTION

The WHO used the under-five mortality rates to estimate that there were 1.4 million blind children globally in 1999.^{1,2} Each year there are an estimate of 500 000 new cases of blind children.³ Childhood blindness is attributed to a group of rare diseases in children and accounts for 3% of the global blind population. However, as these children will have a lifetime of blindness, their number of blind person years worldwide is second only to cataract,¹ with significant economic, social and healthcare costs to the individuals and their

Key messages

What is already known about this subject?

- ▶ The key informant method has been used effectively in many other developing countries and in small scale areas of China to detect the prevalence of childhood blindness and severe visual impairment (BL/SVI). Girls were found at the higher rate of BL/SVI than that at boys in most of the previous studies.

What are the new findings?

- ▶ Prevalence of childhood BL/SVI was low (0.30/1000) and there was no difference on the prevalence of BL/SVI or on the uptake of eye examination among boys and girls in Huidong County, South China.
- ▶ The low prevalence could still be halved with better health education, earlier operation on children with cataract and establishment of surveillance system on health including visual impairment.

How might these results change the focus of research or clinical practice?

- ▶ Further researches could be on testing how the interventions of health education reduce prevalence of BL/SVI in long term follow-up and to detect the possible impact of earlier operation on children with cataract on reducing prevalence of childhood blindness.

families. In 1999, the International Agency for Prevention of Blindness (IAPB) initiative established eliminating childhood blindness as one of the five target priorities.^{1,4}

Prevalence of childhood blindness and severe visual impairment (BL/SVI) in children varies with socioeconomic situation, from 0.3/1000 children in affluent areas to as high as 1.2/1000 in very poor areas.^{1,5} It is estimated at around 10% of the prevalence of the BL/SVI in the local population including all the age groups, which is around 0.43% in China.⁶ The main causes of blindness in children are particularly cornea and lens opacities in developing countries,

while retina and optic nerve dysfunction predominate in developed countries.⁵ Forty-five per cent of the childhood blindness were estimated to be avoidable² globally.

China is the home to 1.38 (2016)⁷ billion people, of whom 244.4 (17.7%) million aged 0–15, with an estimate of 210 000 blind children in 2007.⁸ Previous studies on blindness in children established that the prevalence of BL/SVI was around 0.3/1000 in middle-income areas in 2010⁹ with approximately half of the blindness was avoidable.¹⁰ Due to the initiative of Childhood Cataract Program of the Chinese Ministry of Health in December 2010, tertiary hospitals had been operated substantially on congenital cataracts with subsidies from government by responding to the initiative,¹¹ therefore we anticipate a potential reduction in the proportion of childhood blindness due to congenital cataract since then.

Huidong is located in the eastern coast of Guangdong Province in southern China with a population of 883 454 (2015), who live in 14 towns. Although Guangdong is regarded as a relatively affluent province in China, there are significant inequalities, with average per capital income in some rural areas being just one-fifth of that in the most affluent urban cities in the province.¹² Huidong ranks at middle level of economic situation in the province.

Huidong County People's Hospital (HDCPH) as the secondary level hospital is the only local place where people are able to access general eye services including treatment of cataract, glaucoma and laser photocoagulations on retina. Children with tiny eye problems like conjunctivitis could be helped at outpatients department in Huidong. Any intraocular operations requirement for children would be referred to tertiary hospitals which are at the distance of one to three hours drive. Refraction without glasses dispensing is available in HDCPH, while the patients' family could choose to obtain glasses from optic shops in the town.

The purpose of this study is to assess the prevalence and causes of BL/SVI in children in Huidong County, South China, using key informant method (KIM). Survey of childhood blindness prevalence using the ordinary population based epidemiological sampling methods are generally not feasible because it is a very rare condition and would require a very large sample size to estimate the prevalence. The KIM uses properly trained staffs from communities, who came from the communities. The trained key informants (KIs) do preliminary detection on any suspected children, whose parents felt were blind or having visual impairment, for example, an infant with no social smile or a toddler that bumps into objects while walking, in communities. Each of the KI is able to detect around a dozen of communities in the study period and then refer children suspected with BL/SVI to hospital for further ascertainment. The KIM has been used effectively to estimate the prevalence of childhood blindness in Bangladesh,¹³ China,¹⁴ Malawi,^{15 16} Ghana,¹⁷ Iran,¹⁸ Tanzania¹⁹ and Indonesia.²⁰

There had not been any studies on prevalence of BL/SVI in children conducted in Huidong by the time of this one.

METHODS

This cross-sectional study was ethically approved by Zhongshan Ophthalmic Center, Sun Yat-sen University (ZOC) ethics committee. All participants being referred for further examination in hospital, aged 15 and under were interviewed in the presence of a caregiver who provided written consent. The research adhered to the tenets of the Declaration of Helsinki.

The WHO's definition of BL/VI was used, that is, blindness (BL) is defined as best-corrected visual acuity (BCVA) worse than 0.05 on better eye, and severe visual impairment (SVI) as BCVA equal to or better than 0.05 but worse than 0.1 on better eye. Children with BCVA equal or better than 0.5 on better eye are regarded as normal. Children with BCVA worse than 0.5 but equal or better than 0.1 on better eye regarded as visual impairment.

We selected 10 of the 14 administrative areas (towns) in this study (table 1), after consultation with HDCPH and the county bureau of health. The public health doctors from township level and village doctors from communities are composited as the primary healthcare team in China, who are either registered as medical general practitioners (doctor) or assistant doctors. They were selected as the key informants (KIs) (table 2) and were trained to do preliminary visual acuity (VA) test on children in the communities. The total population of the selected 10 towns in the study was 624 179. The remaining four towns in Huidong County were unavailable to participate in the study due to being involved in other health campaigns at the time when this study went on.

A senior ophthalmologist provided training in each of the 10 towns with 20 to 40 KI participants. The training included basic general ophthalmology knowledge, VA assessment in children, principles of childhood blindness prevention in primary care and referral procedures to paediatric ophthalmology service. The trained KIs went back to their own communities, talked with the head of each village, families with children about the study to spread the news and had bulletins posted in communities, later tested VA for any suspected children.

The KIs ensured that every family in the communities acknowledged of the study and the scheduled time of eye examination in county hospital, before they finished screening in the village. They might contact the senior ophthalmologist for any queries needed.

For children failing to count fingers at 5 m with both eyes in good illumination, they were then referred by KIs for further examination in county hospital on the days announced.

Visual chart, torch, bulletins and posters were supplied to the KIs. The bulletins outlined principles of prevention of childhood blindness and the scheduled examination dates for children in HDCPH. We publicised children's

Table 1 The characteristics of the 10 study areas

Name of the town	Total population	Number of children aged 15 and below	Distance to the County hospital (km)	Number of KIMs trained	Average number of people searched by each KI trained	Number of children examined by specialist	No. of BL/SVI children
Pingshan	170 695	38 165	<1	44	3879	41	4
Daling	61 472	13 727	13	24	2561	22	4
Renshan	75 671	16 942	30	37	2045	18	4
Jilong	38 850	8713	45	36	1079	13	5
Huangbu	39 554	8860	52	51	776	24	2
Duozhu	106 429	23 887	20	45	2365	22	8
Baipenzhu	22 661	5068	30	23	985	8	0
Andun	64 550	14 547	45	32	2017	23	8
Gaotan and Baokou	44 297	9907	90	22	2014	3	2
	624 179	1 39 816		314	1988	174	37
Welfare house*	24	24	0.5	0	0	24	5
Special school†	35	35	<1	0	0	35	0
	624 238			314	1988	233	42

*14 of them were male, 1 had disabled people's certificate, 3 of the BL/SVI were very sick.

†16 of them were male.

BL/SVI, childhood blindness and severe visual impairment; KI, key informant; KIM, key informant method.

eye examination dates and the aim of finding children with BL/SVI through social media platform of HDCPH, Huidong County Government as well as posters.

Census data (2016) were supplied by the County Bureau of Public Security, who renews the data annually, grouped in the format by towns, by every 5 year old and by sex.

All children who attended for examination at HDCPH received measurement of VA and BCVA test with LogMAR chart and refraction cyclopedic. VA was converted into decimal on normal practice in China. Torch, slit lamp, indirect fundus ophthalmoscope and other examination

tools were used to determine diagnosis of the eye. If both eyes had BCVA worse than 0.1, more detailed eye examination was applied and questions on history of mothers' pregnancy and children's growth were raised to the parents/guardians accompanied. The study lasted for 2 months in early 2017.

WHO's form 'WHO/PBL EXAMINATION RECORD FOR CHILDREN WITH BLINDNESS AND LOW VISION'²¹ was used for data collection for children with BCVA worse than 0.1 in this study.

Children aged 0–15 years in the county welfare house and special school were examined by paediatric ophthalmologists. To compare the recorded BL/SVI information with the children referred by the trained KIs, the records for children with BL/SVI and with or without multiple disabilities in the Huidong County Disabled People's Federation (HDCDPF) system were reviewed. The study team visited also Guangzhou City Blind School, the only blind school in Guangdong Province, to search for any children with BL/SVI from the study areas. Huizhou City (prefecture level between county and province) special school was also contacted by phone calls to check whether there were children aged 0–15 with BL/SVI from the 10 study areas.

For non-attenders at the hospital, local doctors performed outreach examinations in the patients' homes. The study team went back to 10% of communities in the study areas to check whether there were any children with BL/SVI missed by KIs and found no additional children with BL/SVI to those referred by KIs.

Table 2 The characteristic of the key informants trained

	n	%
Male of key informants	227	72.3
Range of age	21–65	
Average age (years old)	41	
Average years worked for medical services	17.4	
KIs served for 1–5 years in medical care	43	13.7
KIs served for 6–10 years in medical care	42	13.4
KIs served for 10–15 years in medical care	36	11.5
KIs served for 16–20 years in medical care	37	11.8
KIs served for over 20 years in medical care	146	46.5
KIs without formal medical education	10	3.2
Total number of key informants trained	314	100.0

KIs, key informants.

Table 3 List of children came and were detected in the County hospital who were referred by the trained KIs or came by themselves

Total number of children came to the County hospital	298
Number of children came from the 10 study areas	174
Age range of the 174 children	2 month to 15 years old
Number of boys from the 174 children	110 (63.2%)
Number of children with normal visual acuity	30 (17.2%)
Number of children with refractive errors only	80 (46%)
Number of children who were with strabismus	29 (16.7)
Number of children who were amblyopia plus other problem(s)	24 (13.8%)
Number of children who had visual acuity below 0.1	11 (6.3%)
Total number of children from the 10 study areas being examined	174 (100%)

KIs, key informants.

All statistical analyses were performed using a commercially available software package (Stata 13.1, Stata, College Station, Texas, USA).

RESULTS

The County census data in 2016 showed that there were 139 816 (22.4%) children aged 0–15 years among the total of 6 24 179 dwellers in the 10 study areas in Huidong. We trained 314 KIs from the 10 areas in total (table 1). On average, each key informant searched for children within a population of 2000. All the selected towns are within 1 hour driving distance to the County City and are in good road connection.

Two hundred and twenty seven (227, 72.3%) of the KIs trained were male (table 2). Forty-three (43, 13.7%) KIs had medical background and been worked in primary healthcare for 1–5 years, almost half (146 accounted 46.5%) of them had been served for over 20 years in primary healthcare.

We examined 298 children aged 0–15 on the three scheduled days (table 3), who were referred by the trained KIs or came by themselves, 174 of the 298 children were from the study areas, the remaining 124 children were from other towns not being involved in the study. Of 174 children examined, the age range was from 2 months to 15 years, 110 (63.2%) were boys, 30 (17.2%) had normal VA. Almost half of the 174 examined children had refractive errors. Strabismus and amblyopia together accounted for around 30%. Eleven (6.3%) of them had BCVA worse than 0.1 and received detailed eye examination with pupil being dilated on individual situation.

Table 4 List of the places where the blind and severe visual impairment children were found

Places the BL/SVI children found	Number
Children with BL/SVI came to hospital and were from the 10 study areas	11
Children with BL/SVI and being from local Welfare House	5
Children being examined earlier in other programmes with detailed records	8
Children being registered in system and examined by local doctors	15
Children with BL/SVI from local special school	0
Children being found at the training and referred by KIs	3
Total	42

BL/SVI, childhood blindness and severe visual impairment; KIs, key informants.

Five of the 24 children (14 males) (table 4) in welfare house were found with BL/SVI including three seriously sick children with other chronic conditions. None of the 35 children (16 males) in the county special school (table 4) suffered from BL/SVI. The team also found three of the five postoperative cataract children with BCVA worse than 0.1 at the training of KIs, who were referred by the local doctor.

Eight children with BCVA below 0.1 were examined by the local doctor in earlier 2017 at the vision screening project with all their detailed medical records in the hospital (table 4). They were informed of not coming again to hospital. Another 15 children with BL/SVI were referred by KIs and examined by the local doctors because they did not come on the three scheduled days in HDCPH; all these 15 children had been registered in the HDCDPF system for disabled people with detailed personal medical information.

In total, 42 children were found to be blind or severely visual impaired with VA below 0.1 among the 139 829 children aged 0–15, which established the prevalence of BL/SVI as 0.30/1000 (95% CI 0.27 to 0.33/1000). Thirty-seven (88.1%) of the children with BL/SVI were certified as disabled people in the HDCDPF system and had been receiving welfare benefit. Two children were in school for blind children and one in school for non-blind children. Five were in Welfare house, and 29 (69.0%) children with BL/SVI stayed at home with their families.

Twenty-three (23, 54.8%) of the children with BL/SVI were male (table 5). There was no significant difference on prevalence of BL/SVI among boys and girls. Eight (8, 19.0%) of 42 children with BL/SVI were 0–5 years old, 17 (40.5%) aged 6–10 and another 17 (40.5%) were 11–15 years old, which established that the prevalence of BL/SVI at each of the three age groups was 0.17/1000 (95% CI 0.15 to 0.19), 0.33/1000 (95% CI 0.30 to 0.36) and 0.43/100 (95% CI 0.40 to 0.46), respectively. There was a significant trend across age levels ($p=0.01$). Twenty-four

Table 5 Prevalence of BL/SVI at children, by gender and by age groups

		N	%	P value	95% CI	P value
Gender	Male	23	54.8	0.31/1000	0.28 to 0.34	0.796
	Female	19	45.2	0.29/1000	0.26 to 0.32	
Age (years)	0–5	8	19.0	0.17/1000	0.15 to 0.19	0.001
	6–10	17	40.5	0.33/1000	0.30 to 0.36	
	11–15	17	40.5	0.43/1000	0.40 to 0.46	
Corrected visual acuity of better eye	NLP–0.02	24	57.1			
	<0.02–0.05	10	23.8			
	0.05–0.1	8	19.0			
	Total number of children	42	100.0	0.30/1000	0.27 to 0.33	

BL/SVI, childhood blindness and severe visual impairment; NLP, no light perception.

children (24, 57.1%) had the BCVA worse than 0.02, 10 (23.8%) had BCVA from equal to 0.02 to worse than 0.05 and 8 (19.0%) from equal to 0.05 to worse than 0.1.

By anatomic site diagnosis, nine children with BL/SVI were due to anterior segment disorders and the remaining 33 children were diagnosed with BL/SVI from the whole eye globe or posterior segment problems (table 6). The

Table 6 Causes of blindness and visual impairment of the children identified

Causes		n	Proportion (%)
Site diagnosis	Glaucoma	2	4.8
	Cataract (postoperative)	7	16.7
	Posterior segment	22	52.4
	Optic nerve or CNS	3	7.1
	The whole eye globe	8	19.0
Aetiology diagnosis*	1. Hereditary	19	45.2
	2. Possible intrauterine factor	16	38.1
	3. Perinatal/neonatal factor†	2	4.8
	4. Childhood factor	0	0.0
	5. Cannot determine	5	11.9
Whether with additional disabilities	With additional disabilities	4	9.5
	Without additional disabilities	38	90.5
	Total number of children	42	100.0

*TheBother were ROP.

†Items 2 and 3 under aetiology diagnosis are regarded as potentially avoidable.

CNS, central nerve syndrome; ROP, retinopathy of prematurity.

causes were identified by aetiology, as hereditary in 19 (45.2%) children and were suspected as intrauterine factor in 16 (38.1%). There were two cases (2, 4.8%) of retinopathy of prematurity (ROP). Ten (10, 23.8%) children were affected in multiple sites on their eyes.

All the 42 children detected with BL/SVI in this study had been previously examined and treated by eye specialists. There was one glaucoma child who was recommended for an operation but did not progress due to uncertainty around surgical results and affordability. The remaining 41 children had received the required treatment on the medical diagnosis of the disorders. All the seven children with cataracts had received operations, without significant VA improvement to better than 0.1.

Using the above prevalence, the extrapolated number of children with BL/SVI aged 0–15 in the whole Guangdong Province in 2017 would be 5766 (95% CI 5190 to 6343), on the census data in the year.²²

DISCUSSIONS

This study found a low prevalence (0.30/1000, 95% CI 0.28 to 0.34/1000) of BL/SVI at the age of 0–15, in 10 of the 14 areas of Huidong County, South China in early 2017. Eighteen (42.9%) of the 42 children with BL/SVI were identified as being affected at intrauterine and perinatal/neonatal stage, which are regarded as potentially avoidable.

This study involved 314 public health staffs from township health units and village doctors from communities as KIs, in addition to revision of hospital records and government registration system for people with recognised disability. The study team detected all the children at county well-fare house, county special school.

The remaining four towns in Huidong County that did not participate were more affluent; therefore, prevalence of BL/SVI in children should be equal to or be lower than that in the 10 study areas, although we could still encounter bias by the selection of the study sites without randomness.

The low prevalence of childhood BL/SVI detected in this study is consistent with other study results in China,¹⁴ and some other economically equivalent Eastern-Asian countries like Mongolia²³ and Vietnam,²⁴ but lower than that in India,²⁵ Indonesia²⁰ and African Ethiopia.²⁶

The trained KIs in this study were from the communities, knew well of families and spread the news about the study on a couple of days before they approached children in the communities for VA screening. Most of them had been serving as medical staff for many years and are treated as reliable people by local dwellers. These would help them avoid children with BL/SVI missed from the screening.

The low prevalence of BL/SVI ascertained in children in this study could possibly be attributable to the following reasons. Consanguineous marriage increases BL/SVI chance, like in some South-eastern Asia countries;^{20, 27} however, it is illegal in China. People would not choose relatives as consorts in the modern realities. The one child policy before January 2015 in China led to better general care to the pregnant women and babies to reduce the chance of unnecessary accident, exposure to harmful environment and better nutrition to them. These also explain why we did not find any children with BL/SVI related to the childhood growing-up stage (table 4). According to the local health officer, general physical examinations are mandatory to couples before marriage. The hereditary risks of having babies would be informed before marriage if any of the new couples were found with hereditary problem. Physical examinations are also encouraged to women before and during pregnancy. For pregnant women, routine test on leucorrhoea, blood and urine, thyroid Function Test, Toxoplasma, Tubella, Toxoplasmosis, other viruses test and B-scan are included. Abortion would be arranged to avoid hereditary diseases. The public general health service had been enhanced enormously since 2015 across the country including Huidong, so that public awareness of having healthier babies should be consequently improved. Another reason of the low estimate prevalence was that we did not find any case affected by lack of nutrition, neither any case by infections at perinatal or childhood stages. We found much less children at the age of 0–5 with BL/SVI compared with those at older age group. This could attribute to (1) the children were too young at the age group to be found with BL/SVI; (2) some of the diseases, especially hereditary diseases like retinoblastoma, Leber's Disease, Familial Exudative Vitreoretinopathy (FEVR), pigmentary degeneration of retina and so on, may not reduce VA until later stage. The last reason of low prevalence of BL/SVI in children found in this study could be possibly because some of the children with BL/SVI died soon after they was born, especially those with multiple disabilities.^{5, 28}

The prevalence established in this study could be underestimated. According to the village doctors, people normally preferred not telling in public that there was a child with BL/SVI at home if they thought the family

was able to manage with this child at home. This could possibly explain why we found more children (24, 57.1%) with VA worse than 0.02, but less (one-third of those with VA below 0.02) with better VA from 0.05 to 0.1 (table 5). Although at the training of KIs, we emphasized on the definition of BL/SVI we should use for the study, that is any children with VA below 0.1 were the study subjects, who should be referred for further examination in the hospital, most of the local people still believed that blindness and severe visual impairment means "unable to have light perception or those people who were unable to walk independently". Although we checked again with all the trained KIs through Wechat (a free mobile phone programme for communication by chat, call or information sharing) or phone call to ensure that all children with BL/SVI found should be examined/recorded in the study, we still suspect that few visually impaired children with better VA than blindness might not come for further examination in this study, and neither were registered in the government system nor were examined by the local eye doctors previously with records in the local hospital.

Children aged below 1 year old without notable eye problem but possibly having SVI could also be missed in this study as they could not communicate properly with parents and KIs.

The estimated prevalence could be close to the real rate. Using the surveillance system methodology in the UK,²⁸ the incidence of BL/SVI in those aged 0–5 were expected to be higher compared with older age groups, but the actual prevalence from each group was equal to each other, with those deceased at the age group of 0–5 and being taken out of the prevalence calculation. Based on this assumption in UK, the number of children with BL/SVI at the age of 0–5 in Huidong should be equal to that at older groups numbered as 17 children (table 5) in our study, but we found only 8 (9 less than the assumption) in this study. If we assume to add another 9 more children to the number at this group, it would bring the prevalence from 0.30/1000 to 0.36/1000, which does not make significant difference on the prevalence of children aged 0–15, although there was significant difference between 0–5 and other two groups of 6–10 years and 11–15 years.

There came more boys (63.2%, table 3) to county hospital for further examination from the 10 study areas. The possible reason might be that boys are more outgoing than girls, and no one believed that there was gender discrimination affected less girls to the examination, according to the local doctors and health authorities.

All the children with cataract found in this study were operated at tertiary hospitals with proper treatment and follow-up, while none of them were operated before 2 years old. Late operation on congenital cataract could lead to the development of amblyopia. Children who were with postoperated congenital cataract did not gain significant VA improvement and could also be potentially affected by multiple disorders. This reminds the need for public awareness of early detection of children's eyes and

treatment of congenital cataract to help the development of VA at younger stage.

Our study established a high rate of blind or severely visual impaired children not going for school education. This should call attention from related departments on how to help with these children having their right of education. The authors learnt after this study that there is only one school for blind children in the whole Guangdong Province with around 100 million population. Parents do not pay any tuition fees for primary education in school for blind children, but one of the family guardians has to accompany their child in the school for caring, which becomes the barrier to most of the families with BL/SVI children, as commented by the teachers from Guangzhou school for blindness.

CONCLUSION

This study documented a low prevalence of blindness and severe visual impairment in children aged 0–15 in South China. Almost half of them were still potentially avoidable with better health education, care of pregnancy and care of children's eye. Establishment of surveillance system for disabled children including those with BL/SVI across the country and better health education to the public with the surveillance health outcomes would help the reduction of avoidable BL/SVI further.

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Contributors BX: study design, training of the key informants, monitoring the data collection, data analysis as well as manuscript drafting and revision. YL: draft of the manuscript, data analysis and critical revision of the manuscript. JY, ZW, WH, YZ, SH, XT, JY: design of the study and valuable comments on the manuscript. LJ: statistics analysis and helpful revision. JY: designing and revision of the manuscript.

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Competing interests None declared.

Patient consent Not required.

Ethics approval Ethics approval was obtained from Zhongshan Ophthalmic Centre, Sun Yat-sen University. The approval reference number is 2017KYPJ086. All the children examined at county hospital gave written consent in the presence of their caregivers.

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