Risk Factors of Ocular Anomalies in Down Syndrome Patients in Hospital Cancelor Tuanku Muhriz, UKM

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ABSTRACT

Introduction: The association between advanced maternal age and some possible risk factors of Down Syndrome had been established. However, there is limited research on the risk factors of ocular anomalies among Down Syndrome. Thus, this research aimed to determine the possible risk factors associated with the cases of ocular anomalies among Down Syndrome. Methods: This retrospective study consists of 97 patients who attended the Child Development Clinic in Hospital Canselor Tuanku Muhriz. Results: About 54.6% were recorded to have ocular anomalies. The astigmatism was 39.4%, followed by hyperopia (28.7%). Myopia, anisometropia and strabismus had similar percentages with 11.7% and nystagmus was only reported in 6.4% of patients. The result showed no statistically significant association between the risk factors of advanced maternal aged (p=0.574), advanced paternal age (p=0.591), history of foetal death (p=0.579) and history of maternal illness during the gestation period (p=0.843) with ocular anomalies. However, the subjects with a maternal history of foetal death were 44% more likely to have the risk of ocular anomalies than Down Syndrome patients whose mother did not have any foetal death history. Conclusion: The maternal age, paternal age, history of abortions or stillbirths and history of maternal illness during the pregnancy of Down Syndrome infants were not associated with the presentation of ocular anomalies in Down Syndrome.
Keywords: Risk factors, Ocular anomalies, Anisometropia, Strabismus, Down Syndrome

METHODOLOGY

The retrospective study was conducted at Hospital Canselor Tuanku Muhriz (HCTM) Pusat Perubatan Universiti Kebangsaan Malaysia (PPUKM) among Down Syndrome patients from 2011 to 2018. The lists of Down Syndrome patients from January 2011 to December 2018 were reviewed from Down Syndrome patient attendance lists of Child Development Clinic (CDC) department. From the attendance lists, a total of 302 patients were screened for having Down Syndrome. Then, the patients with a similar medical record number or similar name were considered as duplicate subjects and were counted as one. 142 suitable subjects out of 302 patients on the list were identified and those medical records were requested from the main medical records department of HCTM PPUKM. Only 97 patient files were analysed for the data collection.

RESULTS

Table I: Demographic data of Down Syndrome subjects

Variables	Subjects (%)
Gender	
Female	48 (49.5%)
Male	49 (50.5%)
Race	
Malay	73 (75.3%)
Chinese	20 (20.6%)
Indian	4 (4.1%)
Age [mean ± SD (max – min)]	8.07 ± 4.50 (1 – 19) years
Birth weight [mean ± SD (max – min)]	2.73 ± 0.50 (1.50 – 3.87) kg
Available data	88 (90.7%)
N/A	9 (9.3%)
Gestation period [median (max – min)]	37 (32 – 41) weeks
Available data	82 (84.5%)
N/A	15 (15.5%)
Mode of delivery	
Normal Vaginal Delivery	55 (56.7%)
Lower Segment Caesarian Section	34 (35.1%)
N/A	8 (8.2%)
Presentation of ocular anomalies	
Yes	53 (54.6%)
No	41 (42.3%)
N/A	3 (3.1%)

Table 2: Course of refractive errors at last examination

Age (years)	No	Myopia (D)		Hyperopia (D)		Astigmatism (D)		Anisome-tropia	
		n, (range)	%	n, (range)	%	n, (range)	%	n	%
≤ 5	31	1, (-2.00)	3.2	5, (+1.50 to +4.50)	16.1	5, (1.00 to 2.50)	16.1	1	3.2
6 – 10	37	3, (-4.75 to -6.50)	8.1	16, (+1.50 to +7.00)	43.2	19, (1.00 to 3.00)	51.4	4	10.8
11 – 15	18	5, (-1.75 to -4.00)	27.8	3, (+2.00 to +6.00)	16.7	7, (1.00 to 2.50)	38.9	3	16.7
≥ 16	8	2, (-2.50 to -3.00)	25	3, (+4.75 to +8.25)	37.5	6, (2.50 to 4.00)	75	3	37.5

Table 3: Crude and adjusted odd ratio between the risk factors and ocular anomalies

Variables		Crude		Adjusted	
		Odd Ratio (95% CI)	P value	Odd Ratio (95% CI)	P value
Maternal age	≤ 34 years (references)	1.00		1.00	
	≥ 35 years	0.64 (0.27-1.53)	0.312	0.68 (0.17-2.65)	0.574
Paternal age	≤ 34 years (references)	1.00		1.00	
	≥ 35 years	0.58 (0.23-1.49)	0.260	0.70 (0.19-2.56)	0.591
Foetal death	No (reference)	1.00		1.00	
	Yes	1.11(0.39-3.17)	0.849	1.44 (0.39-5.35)	0.579
Maternal illness	No (reference)	1.00		1.00	
	Yes	0.86 (0.34-2.13)	0.735	0.91 (0.35-2.34)	0.843

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INTRODUCTION

The incidence of birth defects among infants in Hospital Kuala Lumpur, Malaysia, from January 1999 to June 2000, reported that Down Syndrome occurred approximately 12.6 in 10000 births (Noraihan et al. 2005). Research by Genetic Centre in Malaysia showed that of karyotype patterns observed in 149 cases of Down Syndrome, the most common genetic patterns were nondisjunction trisomy 21, affecting 94.6% of the subjects (Azman et al. 2007). Malaysia reported that the average maternal age of Down Syndrome children was 32.3 years, and out of 149 Down Syndrome cases, 64% were born to mothers aged older than 35 years old (Azman et al. 2007). However, several other possible risk factors have also been found to be associated with Down Syndrome, including advanced paternal age (Fisch et al. 2003), history of diabetes mellitus in the mother (Narchi&Kulaylat 1997), the mother's educational level (Khoshnood et al. 2004), history of spontaneous abortions (Bianco et al. 2006), a short interval between pregnancies (Jongbloat&Vrienze 1985) and parents' consanguinity marriages (Shalaby 2011). The risk factors of Down Syndrome itself is considered as a potential proxy of risk factors in those with ocular anomalies in Down Syndrome.The risk factors leading to Down Syndrome are probably are similar to those in ocular anomalies cases. There was limited research regarding risk factors of ocular anomalies in Down Syndrome. The data of the risk factors of ocular anomalies in Down Syndrome can be a baseline description of ocular anomalies in this selected population and may identify the preventable risk factors, thus, reducing the risk of ocular anomalies in children with Down Syndrome. The objectives of this research are to determine the pattern of ocular anomalies, as well as to assess the risk factors of ocular anomalies in Down Syndrome patients in Malaysia.

DISCUSSION & CONCLUSION

Hyperopia had indicated a greater percentage compared to myopia cases in the present study(Table 1). The pattern of the hyperopia in the present study shows the opposite pattern from the normal pattern of the hyperopia cases among normal children population in Malaysia. A research stated that the hyperopia in the normal population has a lower percentage than the prevalence of myopia with 2.9% and 22.2%, respectively. The astigmatism percentage in the present study was 39.4% out of 94 subjects, which was almost similar with the studies reported from Italy, Korea and Turkey with 28%, 31% and 44%, respectively. The strabismus cases slightly lesser than the percentages of strabismus in other studies in Malaysia due to different technique. The research in Japan stated that the highest percentages of strabismus with 40% (Terai et al. 2018). Another study in the Malaysian population had found about 33% nystagmus cases among the Down Syndrome subjects, which were three times more than the present study (Liza-Sharmimi et al. 2006). The pattern of refractive error in our study showed that the distribution of myopia was the highest in the group subjects aged between 11 to 15 years and the group ageing more than 16 years, with 27.8% and 25% (Table 2). The lowest distribution of myopia was in the age of younger than 5 years old, which was 3.2%. This is suggested that myopia in Down Syndrome was presented more in older subjects than younger subjects. This pattern was also indicated in a previous study, which showed the percentages of myopia rose gradually throughout several groups of age from 4 years old until 16 years old, with 11.7% to 36.4% (Terai et al. 2018). Another study also showed almost similar results with 2 out of 9 (22%) Down Syndrome subjects aged 5 years old and older had higher percentages of myopia cases compared with 7 out of 81 (9%) subjects younger than 5 years old (Afifi et al. 2013).For hyperopia, the highest percentages were found in the group of age 6 to 10 years and the group of age older than 16 years old, with 43.2% and 37.5%, respectively. The reason for the inconsistencies in the hyperopia cases in our study may be due to the failure of emmetropisation. The Down Syndrome patients in a longitudinal study were found that the mean hyperopia power during the preschool age had no noticeable changes compared with the mean hyperopia power during the teen age (Al-Bagdady et al. 2011). Based on our odd ratio results in Table 3, the mothers and fathers aged more than 35 years old showed the reduction of risk in ocular anomalies among the Down Syndrome patients by 30%. The results were different compared to the association between the risk factors and the Down Syndrome incidence. There was also a research showing that the advanced paternal age contributed to the incidence of Down Syndrome cases. The foetal death history shows the increment of the odd ocular anomalies development by 44% when the maternal age, paternal age and maternal illness status become the cofounder factors. The risk factors of the history of abortion and Down Syndrome born in comparison with normal infants was indicated in the previous study. They had shown the increased risk of having Down Syndrome babies in the following pregnancy by 47% in 3 or more spontaneous abortion history compared with the mother with no history of abortion (Bianco et al. 2006). Thus, the present study suggested that the incident of ocular anomalies among Down Syndrome may be contributed by the status of the mother's history of foetal death. In conclusion, this study showed that astigmatism and hyperopia were the most common types of ocular anomalies, followed by myopia, strabismus, nystagmus and anisometropia. There were also no statistically significant results found between advanced maternal and paternal age, history of foetal death and the maternal illness during pregnancy and the risk factors of ocular anomalies among the Down Syndrome patients.