International Journal of Medical and Health Research
ISSN: 2454-9142
Impact Factor: RJIF 5.54
www.medicalsciencejournal.com
Volume 3; Issue 11; November 2017; Page No. 116-120

Risk factors for developing different subtypes of strabismus in a Saudi population

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Abstract
Aim: To describe the distribution of different strabismus subtypes and identify potential risk factors.
Methods: A telephone-based survey, interviewing guardians of known strabismus' patients, diagnosed and followed at King Abdulaziz University Hospital, in Jeddah-Saudi Arabia.
Results: We included (113) patients with a mean age at diagnosis of (49.37±52.41) months. Males constituted (50.4%), and most participants were Saudi nationals (64.6%). The top three subgroups encountered were (58.4%) Esotropia, (28.3%) Exotropia and (10.5%) Hypertropia, (1.8%). A positive past medical history of conditions such as hydrocephalus or congenital anomalies, was associated with developing strabismus (P=0.0001). No significant difference detected between the subgroups for the different modes of delivery, nor for an eventful neonatal history. Half of the participants were born into families with positive parents' consanguinity, and higher strabismus rates were significantly associated with a positive family history. (P=0.0001). Maternal past medical history of chronic conditions or an eventful antepartum history was not associated with developing strabismus.
Conclusion: Congenital anomalies, hydrocephalus, and past family history were associated with developing strabismus. There is a need to install a screening tool for early detection of this disorder.

Keywords: strabismus, eyes' misalignment, esotropia, exotropia and hypertropia

Introduction

Strabismus is a disorder of the eyes' alignment, which causes vision suppression and Amblyopia [1], and accounts for 50% to 73% of all vision loss [2, 5]. Although its onset starts early at childhood, its visual defects may continue into older ages [6]. Globally, Strabismus is one of the most prevalent ocular conditions [7], and is recognized as the most common cause of amblyopia worldwide [8, 11]. The exact cause of this condition is not yet clear, however, previous studies reported higher prevalence of strabismus within the same families, where two or more members were affected, suggesting a strong hereditary association [9-10].

Several studies described the adverse psychosocial effects of strabismus [6, 14-16], and others associated strabismus correction with a significantly positive psychological impact [17, 18]. The latter highlighted the need for assessing "The sensitive period", i.e. the period of high susceptibility to strabismus, along with early detection of amblyogenic risk factors, and both were proven beneficial in reducing strabismus's prevalence and severity [19]. Many risk factors were attributed to strabismus, and were broadly classified into two categories; hereditary-based or environmental based [20]. These included; family history of strabismus, maternal and paternal age, maternal cigarette smoking, pre-eclampsia, multiple gestations, neonatal hypoxia, infant prematurity and low birth weight [21-24]. Others further classified these factors into pre-natal and natal encounters, to determine the association of these factors with the timing of development, and identify the "sensitivity period". On the other hand, studies indicated different associations for different sub-types of strabismus, and thus suggesting multiple pathophysiologic pathways for the disorder [24].

Despite the intensity of this issue, research on strabismus in the region and more specifically in Saudi Arabia remains limited. In this study, we aim to describe the distribution of strabismus subtypes among patients attending a tertiary care center in Jeddah-Saudi Arabia, and identify potential risk factors for the different subtypes of strabismus.

Materials and Methods

This study was a cross-sectional survey conducted at pediatrics ophthalmology clinic in King Abdulaziz University Hospital, in Jeddah-Saudi Arabia. We included all patients diagnosed with congenital strabismus between May and July 2016, irrespective of their gender. Patients suffering from secondary strabismus were excluded. Ethical approval was obtained from the Research Ethical and Technical Committee at King Abdulaziz Hospital, along with all necessary administrative approvals.

Regarding data collection, and after reviewing the literature available on strabismus, we developed a telephone-based questionnaire focusing on possible risk factors associated with this condition. The tool was validated and tested prior to data collection. Telephone numbers of patients diagnosed with congenital strabismus were obtained from their medical records, and the guardians of patients who agreed to participant were interviewed. Questionnaires were completed by trained interviewers who explained the purpose of the

study, the content and details of the questionnaire, and reassured participants about the confidentiality of their personal information. Verbal consent was obtained before starting the interview. The questionnaire was designed to gather information on; A. Patients' demographics: including: date of birth, gender, nationality, B. Family history; which included parents' level of education, occupation, and consanguinity, as well as past family history of strabismus, and number of affected siblings. We also collected data on C. Patients' medical history focusing on; age at diagnosis, type of strabismus and laterality (i.e. side of the error), history of previous surgery, chronic illness, congenital anomalies or other conditions, and eventful neonatal history if any (e.g. neonatal hypoxia or jaundice) Lastly, D. The mother's medical history where guardians were asked to report on the mother's medical history including; smoking, chronic illness and eventful antenatal or antepartum history. Data obtained was coded, crosschecked and entered on spreadsheets on daily basis. Statistical analysis was done using the Statistical Package for Social Sciences (SPSS) version 20. Data was presented as mean and standard deviations for continuous parameters, and as number and percentages for categorical parameters. The comparisons between groups were tested using chi–square test. A (P) value < 0.05 was considered statistically significant.

Results

We interviewed a total of (113) patients with a mean age at diagnosis of (49.37±52.41) months. Males constituted (50.4%) of the total sample, and most participants were Saudi nationals (64.6%). In fact, the latter reported significantly higher strabismus's rates in comparison to non-Saudi patients. (P= 0.002) (Table 1) We classified the participants into subgroups according to the subtype of strabismus as follows: (58.4%) were diagnosed with Esotropia, (28.3%) with Exotropia, (10.5%) with Hypertropia, (1.8%) with Exophoria, and lastly (0.9%) with Esophoria. (Figure 1.A) In order to enhance the scope of this study, we compared every aspect of the analysis across the top three subgroups. i.e. Esotropia, Exotropia and Hypertropia subgroups. For the side of error, (78.8%) suffered from strabismus in both eyes, (10.6%) in the right side, and another (20.6%) in the left one, and rates of bilateral strabismus was found significantly higher when compared to a single eye strabismus (P=0.0001) (Figure 1.B) Guardians of two thirds of participants (77.9%) denied any history of medical conditions related to strabismus, weather ophthalmological or systemic. Yet, the remaining (22.1%) reported the following conditions; Mental retardation (8%) Hydrocephalus (6.2%), Multiple Congenital Anomalies (2.7%), Cataract (1.8%), Dawn Syndrome (1.8%), Retinopathy (0.9%) and finally Glaucoma (0.9%). (Table 1) An eventful past medical history was found significantly associated with developing strabismus (P=0.0001).

Participants were asked about other clinical risk factors of strabismus including; the mode of delivery, whereas mothers of more than two thirds of this sample (71.7%) had vaginal deliveries, and (28.3%) delivered by cesarean section. Although cesarean section rates were higher in the Hypertropia subgroup, we found no significant difference between the groups for the different modes of delivery. Regarding neonatal history, (19.5%) of patients suffered from neonatal jaundice, (13.3%) from neonatal hypoxia, (9.7%) had congenital anomalies and (15%) were admitted to Neonatal Intensive Care Unit (NICU). For the subtypes, those with Esotropia had the higher rates of congenital anomalies (9.4% Vs 9.1% & 8.3%), Hypertropia patients suffered mainly from neonatal jaundice (25% Vs 6.2% & 24.2%), and those with Exotropia were the most admitted to NICU (18.2% Vs 16.7% & 9.4%). None of latter was associated with overall strabismus rates nor with the subtypes, expect for neonatal jaundice which was associated with Exotropia (P=0.019). For patients' surgical history, out of the total and as expected (59.3%) underwent eye surgery, and (6.25%) had shunts done for hydrocephalus. Patients suffering from Esotropia were operated on the most (60%) for eye surgery. (Table 1)

Looking into patients' family history, the mean number of affected siblings for the overall group was (3.66±2.51). More than have of the participants (52.2%) were born into families with positive parents' consanguinity, and this was of similar rates across the three subgroups (53.1%, 53% & 50%). However, we detected no association between the latter and developing strabismus (P=0.638). Out of total patients, (28.3%) reported positive family history of strabismus, and mostly from second degree relatives. Overall strabismus rates were significantly associated with a positive family history. (P=0.0001). Interestingly, all Hypertropia patients showed no positive family history of strabismus. Forty six percent of patients' fathers were holders of a master degree or above, while (42.5%) of mothers were holders of similar degrees. For the overall strabismus rates, the latter two subgroups were significantly different when compared to other educational subgroups. (P=0.0001). On the other hand, fathers of professional occupation (53.1%) had no effect on strabismus, while most mothers were housewives (74.3%), and this was significantly associated with having a child suffering from strabismus (P=0.0001).

Focusing on maternal past medical or surgical history, most mothers (85.5%) were free of any diseases, and the remaining few suffered from the following conditions: Diabetes Millets (3.5%), Asthma (1.8%), Stroke (1.8%), Hypothyroidism (1.8%), Hyperthyroidism (0.9%), Anemia (0.9%), Hypertension (0.9%) and Uterus removal (0.9%). Except for one participant, all mothers were non-smokers (99.1%). (Table 2) We also reviewed the details of the mother's antepartum history including: radiation exposure during pregnancy, infections during pregnancy, medications during pregnancy, antibiotics during pregnancy, trauma during pregnancy, maternal pre-eclampsia, gestational diabetes, multiple gestations, threatened abortion, placenta previa, polyhydramnios, vacuum assisted delivery, abnormal position, prolonged labor, premature labor, premature rupture of membrane and antepartum hemorrhage. Except for threatened abortion association with Exotropia (P=0.035), none of the above conditions was associated with overall strabismus, nor with any of the subtypes. This applied for both chronic illness such as diabetes and hypertension, or any other conditions encountered during pregnancy.

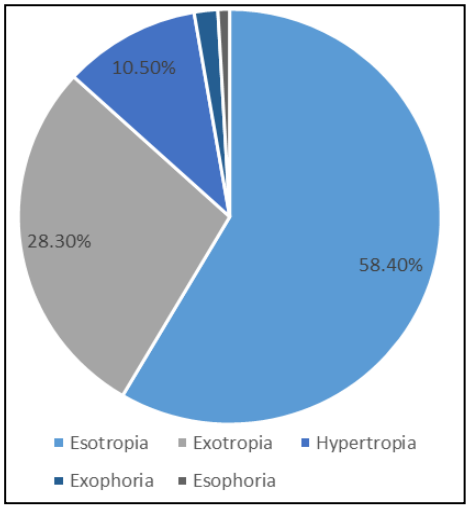

Fig 1(a): Subtypes of Strabismus P Value = 0.0001

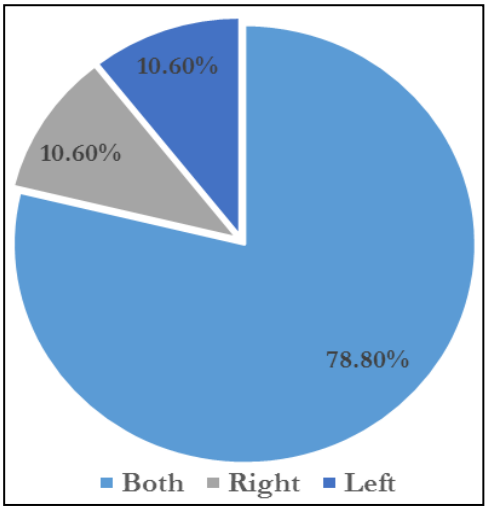

Fig 1(b): Side of Error P value = 0.0001

Fig 1: Subtypes and laterality of Strabismus (Side of error)

Table 1: Patients Characteristics (Demographics, Neonatal, Medical and Surgical History)

Parameters		Overall Strabismus	Subtype of Strabismus		
			Esotropia (n=66)	Exotropia (n=32)	Hypertropia (n=12)
Age at diagnosis* (months)		49.37±52.41	39.79±39.95	70.97±72.56	47.33±40.96
Gender	Male	57 (50.40%)	34 (51.5%)	14 (43.8%)	7 (58.3%)
	Female	56 (49.50%)	32 (48.5%)	18 (56.2%)	5 (41.7%)
Nationality	Saudi	73 (64.6%)	46 (69.7%)	21 (65.6%)	4 (33.3%)
	Non-Saudi	40 (35.4%)	2 (30.3%)	11 (34.4%)	8 (66.7%)
Neonatal History	Neonatal asphyxia	15 (13.3%)	4 (12.5%)	8 (12.1%)	2 (16.7%)
	Neonatal Jaundice	22 (19.5%)	2 (6.2%)	16 (24.2%)	3 (25.0%)
	Congenital anomalies	11 (9.7%)	3 (9.4%)	6 (9.1%)	1 (8.3%)
	NICU	17 (15.0%)	3 (9.4%)	12 (18.2%)	2 (16.7%)
Mode of Delivery	Vaginal delivery	81 (71.7%)	25 (78.1%)	47 (71.2%)	8 (66.7%)
	Cesarean section	32 (28.3%)	7 (21.9%)	19 (28.8%)	4 (33.3%)
Medical history	No	88 (77.9%)	51 (77.3%)	24 (75.0%)	11 (91.7%)
	Mental retardation	9 (8.0%)	5 (7.6%)	3 (9.4%)	-
	Hydrocephalus	7 (6.2%)	6 (9.1%)	1 (3.1%)	-
	Multiple congenital anomalies	3 (2.7%)	1 (1.5%)	1 (3.1%)	1 (8.3%)
	Cataract	2 (1.8%)	1 (1.5%)	1 (3.1%)	-
	Down syndrome	2 (1.8%)	-	2 (6.4%)	-
	Retinopathy	1 (0.9%)	1 (1.5%)	-	-
	Glaucoma	1 (0.9%)	1 (1.5%)	-	-
Surgical history	No	39 (34.5%)	30 (30.3%)	11 (34.4%)	6 (50.0%)
	Eye surgery	67 (59.3%)	40 (60.0%)	20 (62.5%)	6 (50.0%)
	Shunt of hydrocephalus	7 (6.2%)	6 (9.1%)	1 (3.1%)	-

Age is represented in means and standard deviations. All other parameters are presented in counts and percentages.

Table 2: Patients Characteristics (Family History)

Parameters		Overall Strabismus	Subtype of strabismus		
			Exotropia	Esotropia	Hypertropia
No. of Siblings		3.66±2.51	3.94±3.25	3.47±2.16	3.75±1.82
Parents' consanguinity	No	59 (52.2%)	17 (53.1%)	35 (53.0%)	6 (50.0%)
	Yes	54 (47.8%)	15 (46.9%)	31 (47.0%)	6 (50.0%)
Family history of strabismus	No	81 (71.7%)	20 (62.5%)	47 (71.2%)	12 (100.0%)
	Yes	32 (28.3%)	12 (37.5%)	19 (28.8%)	-
	1st degree relatives	12 (37.5%)	4 (33.3%)	8 (42.1%)	-
	2nd degree relatives	16 (50.0%)	7 (58.3%)	8 (42.1%)	-
	3rd degree relatives	4 (12.5%)	1 (8.3%)	3 (15.8%)	-
Father's Education	Master and above	52 (46.0%)	1 (3.1%)	4 (6.1%)	1 (8.3%)
	Bachelor's degree	34 (30.1%)	15 (46.9%)	32 (48.5%)	3 (25.0%)
	High school	21 (18.6%)	12 (37.5%)	20 (30.3%)	2 (16.7%)
	Below high school	6 (5.3%)	4 (12.5%)	10 (15.2%)	6 (50.0%)

Father's Occupation	Professional	60 (53.1%)	16 (50.0%)	36 (54.5%)	5 (41.7%)
	Non-professional	53 (46.9%)	16 (50.0%)	30 (45.5%)	7 (58.3%)
Mother's Education	Master and above	48 (42.5%)	-	1 (1.5%)	1 (8.3%)
	Bachelor's degree	34 (30.1%)	13 (40.6%)	31 (47.0%)	2 (16.7%)
	High school	29 (25.7%)	9 (28.1%)	19 (28.8%)	1 (8.3%)
	Below high school	2 (1.8%)	10 (31.2%)	15 (22.7%)	8 (66.7%)
Mother's Occupation	House wife	84 (74.3%)	23 (71.9%)	49 (74.2%)	10 (83.3%)
	Professional	18 (15.9%)	5 (15.6%)	10 (15.2%)	2 (16.7%)
	Non-professional	11 (9.7%)	4 (12.5%)	7 (10.6%)	-
Mother's Medical History	No	97 (85.8%)	26 (81.2%)	59 (89.4%)	9 (75.0%)
	Yes	16 (14.2%)	6 (18.8%)	7 (10.6%)	3 (25.0%)
	Diabetes mellitus	4 (3.5%)	2 (6.2%)	2 (3.0%)	-
	Asthma	2 (1.8%)	1 (3.1%)	1 (1.5%)	-
	Stroke	2 (1.8%)	-	2 (3.0%)	-
	Hypothyroidism	2 (1.8%)	-	1 (1.5%)	1 (1.5%)
	Anemia	1 (0.9%)	-	1 (1.5%)	-
	Hypertension	1 (0.9%)	1 (3.1%)	-	1 (8.3%)
	Rheumatoid arthritis	1 (0.9%)	-	-	1 (1.5%)
	Hyperthyroidism	1 (0.9%)	1 (3.1%)	-	-
	Uterus removal	1 (0.9%)	1 (3.1%)	-	-
Mother's Smoking History	No	112 (99.1%)	31 (96.9%)	66 (100.0%)	12 (100.0%)
	Yes	1 (0.9%)	1 (3.1%)	-	-

Discussion

Despite the high strabismus rates reported in the region [25], limited research was done in the Middle East and in Saudi Arabia, especially research focusing on the distribution and epidemiology of this disorder. Thus, and despite the availability of literature from other regions, the wide variations of the studied populations may complicate specific comparisons, and allows only for general inferences [25]. In this study, we estimated the prevalence of strabismus, and its different subtypes, and identified potential risk factors in a tertiary care center in Jeddah-Saudi Arabia.

In other population, ethnicity was found significantly related to the distribution of strabismus, and the more specifically of its different subtypes [25]. In our sample, around two thirds of our strabismus's patients were Saudi nationals (P= 0.002), indicating a strong association between the local race and higher rates of strabismus. Strabismus is classified into comitant and non-comitant types, depending on the deviation's magnitude at all gaze positions. Comitant strabismus includes intermittent or constant Exotropia, infantile Esotropia, and accommodative or non-accommodative acquired Esotropia. Exotropia and esotropia are the two main and most common forms of strabismus [23]. for our sample, Esotropia was the most commonly seen subtype (58.4%), followed by Exotropia. This was consistent with another local study in Al-Riyadh, which reported Esotropia as the most commonly diagnosed subtype among their patients. These findings also agreed with other regional studies conducted in Oman [26], and Egypt [27] as the first reported (2.67:1) Esotropia to exotropia ratio in their Omani population [26], and the second estimated a (5:1) Esotropia to exotropia ratio among Egyptian patients [27].

An eventful past medical history in early life was strongly associated with strabismus for this group, including conditions such as hydrocephalus and congenital anomalies. This association was also noted in another study in Denmark, where congenital anomalies were more associated with Exotropia [24]. The same study detected an association between deliveries via cesarean sections and Exotropia only, and excluding other subtypes [24]. For our sample, no association was detected, although higher cesarean sections rates were noted for the Hypertropia subgroup. This may suggest more commonalities in the etiology of Exotropia and Hypertropia. Despite reporting relatively high positive parents' consanguinity in this sample, no association was detected between the latter and developing strabismus (P=0.638), and in contrast to what was reported in previous studies [9-23]. However, this could be explained by the relatively small sample size included this study, and the mild variability it represents. On the other hand, a positive family history of strabismus was strongly associated with developing the disorder. It has been shown that children from poor socio-economical class were more likely to develop many ocular problems including strabismus [22]. This was also noted in this study, where mothers of most patients were non-working housewives, leaving the household's burden on the father, and negatively affecting the family's socio-economic status.

The following limitations should be acknowledged; due to resources constraints, we included only a single center, and focused on previously diagnosed cases, and thus the recruited sample was relatively small. Another problem was the accuracy of history, and issues around recall since information was obtained by interviewing mothers of patients. On the other hand, the study showed many strengths such as: including all subtypes diagnosed, whether controlled or those in need for surgical correction. It demonstrated strong associations with named risk factors in this population, and the latter may support the installment of a context-sensitive and comprehensive secreting tool.

Conclusion

Esotropia was the most commonly encountered strabismus subtype. Congenital anomalies, hydrocephalus, and past family history were all associated with developing strabismus. More research is needed to design and install a context-sensitive screening tool, for an early detection of this disorder.

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