Consanguinity, family history and risk of epilepsy: A case control study

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ABSTRACT

Objective: To assess the association between consanguinity and family history in the risk of developing epilepsy later on in life.

Materials and Methods: A case control study was carried out using data from 234 records comprising cases and controls in the proportion of 1:2. The cases were 76 patients suffering from idiopathic epilepsy, and the controls were 151 diseased patients who were non-epileptics. Data were analyzed using PASW Version 18.0. Chi square test was used to test associations and a binary logistic regression was done to calculate the adjusted odds ratio.

Results: The study population comprised 53.7% males and 46.3% females. 48.3% of the cases were of South Asian origin. The most common age group among the cases and the controls was 11-40 years. Both family history and consanguinity had an association with epilepsy. 81% of cases had a positive family history when compared to the 19% in the controls. The odds ratio was 18.37 (CI= 8.37-40.3). A positive history of consanguinity was observed among 17% of the cases, whereas it was 31% in the controls. The odds ratio was 0.46 (CI= 0.22-0.90). The adjusted odds ratio for family history was 17.7 (CI=8.04-39) and the adjusted odds ratio for consanguinity was 0.53 (CI=0.23-1.19).

Conclusion: There was a significant association between family history and the risk of developing epilepsy, with most of our patients having a positive family history. There seems to be no link between epilepsy and consanguinity.

Key words: consanguinity, family history, risk of epilepsy, UAE

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INTRODUCTION

Epilepsy is defined as a chronic neurological condition characterized by recurrent seizures that are caused by abnormal cerebral nerve cell activity. According to WHO, epilepsy is a chronic neurological disorder that affects people of all ages. Around 50 million people worldwide have epilepsy, with nearly 90% of them living in the developing countries. There is a distinction between a patient who has one seizure and a patient who has epilepsy[1]. One seizure does not signal epilepsy (up to 10% of people worldwide have one seizure during their lifetimes). Epilepsy is characterized by two or more unprovoked seizures.

Epilepsy is a neurological disorder that has a very high incidence all across the world. It is not associated with a high mortality rate[2]. There are various risk factors that could lead to epilepsy. However, a few studies have shown that there is a strong link between epilepsy and consanguinity. Further, population studies revealed an increased familial clustering of epilepsy among first degree and to a lesser degree second degree relatives[3]. There are many investigations that are being carried out on this topic across the world. However, we chose this topic for our study since consanguineous marriages have been a common practice and a socially acceptable custom in the Middle East.

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United Arab Emirates is located in Middle East bordering Oman and Kingdom of Saudi Arabia. Its population body is composed of many ethnicities of which only 16.5% are Emiratis, with 83.5% being expatriates. The total population in the UAE is approximately 5,148,664[6].

The prevalence of consanguinity has increased in the UAE by more than 39% compared to that in the previous generations. The health complications that are associated with consanguinity are caused by the expression of recessive genes inherited from a common ancestor[4]. A person's risk of developing the disorder partly depends on what type of epilepsy the family member has had. Several types of childhood epilepsy, such as benign focal childhood epilepsy, childhood absence epilepsy, and juvenile myoclonic epilepsy, may be passed on from parent to child[5]. Our goal was to find out the association between epilepsy, family history, and consanguineous marriages.

MATERIALS AND METHODS

A case-control study was done with 76 cases of epilepsy and 151 controls, based on the records maintained at two tertiary care hospitals in the UAE. The ratio of cases to controls was 1:2. A case was defined as a diagnosed case of idiopathic epilepsy in a person younger than 45 years of age, as given in hospital records. The cases were selected using consecutive sampling, where every record that fulfilled the case definition was included in the study; controls were patients with no epilepsy from hospital records, who were selected using judgmental sampling.

A proforma was prepared and pilot-tested with six records. For pilot-testing we collected data from the record files of a small sample (three cases and three controls). A few variables such as "degree of consanguinity" and "time of diagnosis since epilepsy" were removed following the pilot-test since the relevant data were not found in any of the record files. Variables included history of consanguinity, family history, age, gender, nationality and the diagnosis of epilepsy.

A letter to seek permission for data collection was submitted to the records section of the hospitals: for cases, the file numbers of patients with idiopathic epilepsy during the previous six months were identified by the neurologists in both the hospitals; for controls, age- and gender-matched files with no epilepsy were chosen from the Internal Medicine patient records. The research protocol was approved by the Ethics Committee of GMU.

Data were analyzed using PASW Version 18.0, and the results presented mainly as percentages. Associations were tested using the Chi square test, and risk estimation done using odds ratio. Binary logistic regression analysis was done to calculate the net effect and adjusted odds ratio.

RESULTS

In this case control study the number of patients with epilepsy (cases) were 76 (33.5%), and the number of patients without epilepsy (controls) were 151 (66.5%). The patients not having the disease condition were double the number of patients having the disease.

Table 1 summarizes the different variables and their distribution between cases (patients with epilepsy) and controls (patients without epilepsy).

Out of a total of 76 cases, the maximum number was observed to be between the ages 21

Table 1. Profile of cases and controls

Variables		Cases		Controls	
		No.	%	No.	%
Age					
	0-10	23	30.3	17	11.3
	11-20	11	14.5	40	26.5
	21-30	27	35.5	38	25.2
	31-40	7	9.2	37	24.5
	41-50	8	10.5	19	12.6
Gender					
	Male	39	51.3	83	55.0
	Female	37	48.7	68	45.0
Country of Origin					
	UAE	12	35.3	22	64.7
	Other GCC	11	29.7	26	70.3
	South Asian	31	29.8	73	70.2
	Other Asians	12	40.0	18	60.0
	African	6	46.2	7	53.8
	Others	4	44.4	5	55.6
Consanguinity					
	Positive	13	17.1	47	31.1
	Negative	63	82.9	104	68.9
Family History					
	Yes	43	56.6	10	6.6
	No	33	43.4	141	93.4

to 30 years (35.5%), and the least in the age group 31 to 40 years (9.2%). Out of a total of 151 controls, the were observed in the age group 11 to 20 years (26.5%), and the least in the age group 0 to 10 years (11.3%). There was no gender predominance observed in our study.

Among the cases almost half of the patients were from the South Asian countries, which included India, Pakistan, Bangladesh and Sri Lanka. A similar pattern was seen among the controls. 17.1% among the cases had a positive history of consanguinity while 31% among controls had a similar history. Among the cases 56.6% had a positive family history of epilepsy, whereas among the controls only 6.6% had a positive family history.

Figure 1 shows the different types seizures that were observed in our study. Generalized Tonic-Clonic was the type of seizure with the highest prevalence.

Table 2 shows that out of the cases 17.1% had a positive history of consanguinity, and among the controls 31.1% had a similar history. Chi square test showed a significant association between controls and positive history of consanguinity with an odds ratio of 0.46. Table 3 also shows that 43 (81.1%) cases had a positive family history of epilepsy, whereas among the controls it was 10 (6.6%), with an odds ratio of 18.37.

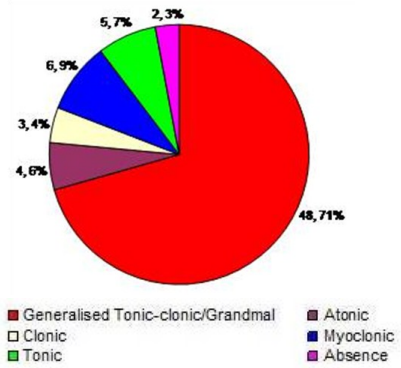

Figure 1. Distribution of different types of seizures

Table 2. Distribution of consanguinity history and family history with disease condition

Variables	Cases No. (%)	Controls No. (%)	Total No. (%)	P
Positive consanguinity history	13 (17.1)	47 (31.1)	60 (26.4)	<0.02
Negative consanguinity history	63 (82.9)	104 (68.9)	167 (73.6)	
Positive family history of epilepsy	43 (56.6)	10 (6.6)	53 (23.3)	<0.001
Negative family history of epilepsy	33 (43.4)	141 (93.4)	174(76.7)	

A binary logistic regression analysis was done to calculate the adjusted odds ratio and the net effect. It was seen that the adjusted odds ratio for family history was 17.7 (CI=8.04-39) and the adjusted odds ratio for consanguinity was 0.53 (CI=0.23-1.19).

Table 3. Risk (Crude and Adjusted) of epilepsy relative to family history and consanguinity

History		OR	CI	Adjusted OR	CI
Family	Negative	1	--	1	--
	Positive	18.37	(8.37-40.30)	17.7	(8.04-39.00)
Consanguinity	Negative	1	--	1	--
	Positive	0.46	(0.22-0.90)	0.53	(0.23-1.19)

CI - Confidence Interval

DISCUSSION

Our study was an attempt to assess the relationship between epilepsy, consanguinity, and positive family history, with a case control study where the ratio of cases to control was 1:2. The data revealed that 71.0% of patients with epilepsy had Generalised Tonic-Clonic seizures.

Consanguinity is very frequently seen amongst UAE citizens, having an incidence of 45-54%[4,7,8]. It has recently been seen to have increased in the younger generations by 28%[4]. However, in our study only 26.4% of the cases had a history of consanguinity. This could have been because 40.8% of the cases were of South Asian origin. The highest incidence of epilepsy was seen to be in the age group of those between 21-30 years, with no gender predominance.

Epilepsy is a distressing disease and might prove to be a social handicap. Our study revealed that 58.9% of the cases were unmarried and only 38.8% were married; epilepsy may have been a contributory factor to this situation. However, this result could have arisen due to the small sample size. A study carried out by Wada et al. showed that idiopathic epilepsy without mental retardation or any disabilities has various negative effects on the patient's social life especially married life[9].

A considerable percentage of our cases (82.9%) had a negative history of consanguinity. This suggests that consanguinity is not a major risk

factor in the development of epilepsy. However, other studies do show a positive correlation between the two. One study, by Ramasundrum and Tan, stated that there was an increased risk of epilepsy in children whose parents have entered into consanguineous marriages and have been diagnosed with idiopathic and cryptogenic epilepsy[10]. This strongly suggests an inheritance pattern in these types of epilepsy. The study by Mehndiratta in Iran on 181 children and adolescents (up to 18 years) also shows that consanguinity is a risk factor for epilepsy. It showed that consanguinity in parents of the epilepsy patients was significantly higher when compared to the general population, indicating that consanguinity is a risk factor for epilepsy. Overall, 33.7 % were first cousins, and 20.7% were second cousins[11]. In a study done by Al-Gazali et al. on the patterns of central nervous system anomalies and consanguineous marriages, it was found that a high frequency of the CNS disorders were caused by recessive genes, some disorders being extremely rare and even not mentioned in the literature[12]. In a study carried out by Chandra V the results indicated that consanguinity increases the frequency of rare recessive CNS disorders in a population[13]. Our study did not significantly indicate a similar result. This could have been due to the small sample size as well as the limited number of consanguinity amongst our cases.

Our study revealed that family history did have a significant link in the contribution to the development of idiopathic epilepsy. 81.1% of our cases had a positive family history. This positive association has also been seen in a study done by Callenbach et al. where the findings confirmed a role for genetic factors in the pathogenesis of epilepsy. This study additionally revealed that the relatives of the patients with idiopathic epilepsy had the same type of seizures[14]. Marini carried assessed the clinical features and genetics of idiopathic epilepsy beginning in adult life, and the pedigree analysis revealed that adult onset idiopathic generalized epilepsy had an underlying genetic aetiology[15]. Another study carried out by Doose et al. stated that family history and EEG of probands and relatives showed that the pathogenesis is determined by genetic factors[16]. In our study 18.9% of the controls had a positive history of epilepsy in their family. Thus there seems to be a strong association in the development of epilepsy among those who have a positive family history. This is reinforced by the adjusted odds ratio of 17.7 (CI=8.04-39) for family history. Therefore, family history appears to have a significant association with epilepsy.

CONCLUSION

The most common seizure in our study was generalized tonic clonic seizure. Both family history and consanguinity had an association with epilepsy.

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