CONSANGUINEOUS MARRIAGE AS RISK FACTOR FOR IDIOPATHIC GENERALIZED EPILEPSY (IGE)

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ABSTRACT

Objective: To determine the significance of parental consanguinity as a risk factor for idiopathic generalized epilepsies.
Study Design: Case control study.
Place and Duration of Study: Outdoor Section of Pediatric Neurology department, The Children Hospital Lahore, from Jan to Dec 2015.
Methodology: A total of 402 patients were included in the study with case to control ratio of 1:1. The 201 cases suffering from idiopathic generalized epilepsy were taken from Pediatric Neurology outdoor and 201 non epileptic patients were taken from general outdoor of The Children Hospital Lahore. All the information was taken on predesigned Profoma.
Results: The percentage of parental consanguinity in case group was 74.1% as compared to 54.7% in control group. Family history of epilepsy among cases was high (24%) as compared to control (10%). The most common type of epilepsy was generalized tonic clonic (GTC) 90.5% with mean age of onset of 5.2 years. The calculated Odd ratio for family history of epilepsy was 2.7 (OR=2.7, CI= 95%, p<0.001) and for parental consanguinity was 3.2 (OR=3.2, CI=95%, p<0.001).
Conclusion: Parental consanguinity was strongly associated with risk of developing idiopathic generalized epilepsy. Family history of epilepsy was another risk factor for the development of epilepsy. The result of this study supports the impact of genetic markers on the transmission of IGEs.

Keywords: Family history of epilepsy, Generalized tonic clonic, Idiopathic generalized epilepsy, Parental consanguinity.

INTRODUCTION

The Idiopathic generalized epilepsy (IGE) is a group of disorder with distinct clinical and electroencephalo-graphic features and constitutes about one third of all epilepsies[1]. It consists of recurrent generalized epileptic seizures without structural brain lesion or interictal abnormal neurological signs and symptoms[2]. IGE can present at any age but it is more common in first and second decade of life[3]. Patients may present with tonic clonic seizures, Absence seizures, Myoclonic seizures and Atonic seizures alone or in combinations[4]. It is considered as large group of epilepsy with undetermined and unknown etiology although genetic origin is the most accepted cause with monogenic and polygenic model of inheritence[1,2]. Familial clustering of epilepsy have been proven among first degree and to a lesser extent second degree relatives and it is higher in case of idiopathic generalized epilepsies[5]. There is increased risk of epilepsy among siblings of patient with idiopathic epilepsy that has parental consanguineous marriage[6].

A consanguineous marriage is referred as a kin marriage among close biological relatives descending from common ancestor[5]. Worldwide, 690 million people are consanguineous and a very high rate of consanguineous marriages are historical and a part of culture in South Asian countries[6,7]. Previous studies suggest that genetic transmission from consanguineous union may lead to emergence of various health issues and there is increased risk of still birth, abortions, congenital malformation, perinatal mortality and genetic disorders[5,6]. While parental consanguinity is a common practice in South Asia but its influence and effect on epilepsy remains underscored because of the limited number of evidence and epidemiological studies[7,8]. So, the better understanding of the effect of consanguineous marriage on the occurrence of epilepsy is quite important as it may raise the public awareness of potential negative effects of kin marriages. The objective of this current study was to evaluate the association between epilepsy and parental consanguinity and to investigate if consanguineous unions contribute significantly to the etiology of epilepsy, which is a common neurological disorder.

IGE are forms of generalized epilepsies in which all seizures are initially generalized (absences, myoclonic jerks and generalized tonicclonic seizures), with an EEG expression that is a generalized bilateral, synchronous, symmetrical discharge (such as is described in the seizure classification of the corresponding type).

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The patient usually has a normal interictal state, without neurological or neuroradiological signs[2]".

"A consanguineous marriage is referred as a kin marriage among close biological relatives descending from common ancestor[5]". Familial clustering of a disease is defined as "The occurrence of the disease within some families in excess of what would be expected from the occurrence in the population[5]".

METHODOLOGY

This case control study was conducted at the outdoor section of Pediatric Neurology department of Children Hospital, Lahore and control group was selected from general outpatient department, from January to December 2015. The calculated sample size by using WHO calculator for sample size determination in health studies was 200 keeping 5% margin of error and 95% confidence level as the prevalence of epilepsy in Pakistan was 9.98/1000 population[3]. Consecutive sampling was done for this case control study and all the known cases of IGE of both the genders up to the age of 12 years, coming to outdoor department were included in the study as the case group and non epileptic children of same age group of both the sexes were included as a control group. Epileptic cases with developmental delay, underlying brain pathology, previous history of CNS infections or trauma, degenerative brain functions, abnormal neurological examination were excluded from the study. Adopted children and children with other chronic illness were also excluded. A written consent from parents/guardian was taken and Information regarding age, gender, age of onset, family history, type of idiopathic epilepsy and parental consanguinity was collected on predesigned Profoma. All the data were entered and analyzed using SPSS-20. For quantitative variables like mean ± SD were presented and for qualitative variables frequency and percentages were recorded.The association between parental consanguinity and family history with the risk of epilepsy was assessed by calculating Odds Ratios and *p*-value ≤0.05 was considered statistically significant.

RESULTS

A total of 402 children were included in the study and out of them case group had 201 epileptic children and control group had 201 non epileptic children. The mean age for the cases was 7.8 ± 2.78 and for the control group was 6.9 ± 2.33. The mean age of onset for IGEs was 5.3 ± 2.62. Gender distribution was not significant, both male and female were equally included in the study (table-I). Distribution of different variables among case and control group is shown in the table-I. The percentage of parental consanguinity was significantly high in case group 74.1% with frequency of 149 as compared to 54.7% in control group with frequency of 110. Family history of epilepsy was also significantly high in case group (24%, frequency 49) as compare to control (10%) with frequency of 21 (table-II). The calculated Odd ratio for Family history of Epilepsy was 2.7 (OR=2.7, CI= 95%, p<0.001) and for parental consanguinity was 3.2 (OR= 2.3, CI=95%, p<0.001). The most common type of epilepsy was generalized tonic clonic (GTC) 90.5% (table-III) with mean age of onset of 5.2 years and the frequencies of different types of idiopathic generalized epilepsy. Parental consanguinity was also more common among cases with GTC epilepsy (75%) as compared to other types.

Table-I: Demographic parameters.

Variables	Case Group		Control Group	
Mean age	7.8 ± 2.7		6.9 ± 2.3	
Parental Consanguinity	149 (74.1%)		110 (54.7%)	
Family History of Epilepsy	49 (24%)		21 (10%)	
Gender Distribution	Male	Female	Male	Female
	104 (51.7%)	97 (48.3%)	100 (49.3%)	101 (50.7%)

Table-II: Parental consanguinity and family history of epilepsy.

		Parental Consanguinity			Family History of Epilepsy	
		Frequency	Percentage		Frequency	Percentage
Case Group	Yes	149	74.1%	Yes	49	24.4%
	No	52	25.9%	No	152	75.6%
Control Group	Yes	110	54.7%	Yes	21	10.4%
	No	91	45.2%	No	180	89.5%
Odd Ratio (OR)	2.3 (95% CI)			2.7 (95% CI)		

Table-III: Types of idiopathic generalized epilepsies.

Types of Idiopathic Generalized Epilepsies	n (%)
Generalized Tonic Clonic	182 (90%)
Myoclonic	8 (4%)
Absence	5 (2.5%)
Atonic	6 (3%)

DISCUSSION

Worldwide the practice of consanguineous marriage is quite variable but it is significantly high in North Africa, The Middle east, South Asia and among migrant community in North America[9]. In a demographic and health survey, the percentage of parental consanguinity in Pakistan is about 51.3-53.1% in urban area and it is 65.6-66.9% in rural areas[10]. It has been proved that consanguineous couples are at high risk of having offspring with genetic disorder[11]. Parental consanguinity is more common risk factor among IGE as compared to symptomatic or cryptogenic epilepsies as IGEs are considered to be genetically transmitted with monogenic and polygenic inheritance[12]. This study was conducted to determine parental consanguinity as a risk factor for idiopathic generalized epilepsies. It was a case control study with case to control ratio of 1:1. In this study the percentage of parental consanguinity was quite high (74.1%) in case group as compared to control group (54.7%) which was in favor of study done in Oran, that recognized consanguinity as significant risk factor for genetically transmitted epilepsies[13]. High rate of parental consanguinity has also been reported among 31 Jordanian families with familial childhood epilepsy and among Iranian epileptic children as compared to general population[12,14]. Family history of epilepsy is also considered as another risk factor for epilepsy especially in case of IGE[15]. The result of this study was also comparable to this as the percentage of family history of epilepsy was quite high (24%) in epileptic children as compared to non epileptic children (10%). Although this percentage was not much high if it is compared to the Jordanian study which reported it as one fourth of the total cases and khan documented it even more high[16-18]. The peak age of onset for IGEs was 5.3 years, although it can be seen in all age group and a bimodal appearance for peak age for IGEs has been observed with small peak at 2 years and a large peak at 15 years[19]. Gender predominance was not significant as male and females were almost equal in number which was comparable to the previous studies as in Cutting's study women out numbered men and in Marin's and Nicolson's studies men outnumbered women in adult onset IGEs[20,21]. But in childhood IGEs a male preponderance has also been observed[19]. The most common type of IGEs in this study was Generalized tonic clonic (GTC). Bendadis also reported IGE with GTC seizures as the largest group and a study done Jordon on inheritance profile of IGEs revealed the same results[23,14]. But Nicolson and Mohanjar reported juvenile myoclonic (JME)epilepsy as the largest group[22,24]. In this study 90% of the epileptic children had generalized tonic clonic seizures and only 4% had myoclonic epilepsy. Reason for this difference cannot be explained and population based genetic studies for specific type of epilepsy are needed to explore the causes. This study was not able to compare parental consanguinity as a risk factor between idiopathic generalized epilepsies and secondary epilepsies, so that an impact of genetic markers on the type of epilepsy can be provided. But still genetic transmission among IGEs can be supported by the high percentage of parental consanguinity among epileptic children as compared to non epileptic children.

CONCLUSION

Parental consanguinity was strongly associated with risk of developing IGE. Family history of epilepsy was another risk factor for the development of epilepsy. The result of this study supports the impact of genetic markers on the transmission of IGEs.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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