

Consanguinity and risk of epilepsy

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Genetic link to epilepsy was established with the twin studies of Lennox.^{1,2} Further population studies revealed an increased familial clustering of epilepsy among first degree and to a lesser degree second degree relatives.² Idiopathic epilepsy has a higher familial clustering of epilepsy.³ Similar association has been seen for cryptogenic epilepsy also in population studies especially for generalised seizure and younger onset of epilepsy.³ Symptomatic epilepsy like intractable HS and SSEL have a reported a family history of seizures/epilepsy of 20-60%.^{4,5} Such high rates may be due to common environmental or common inherited genetic influences. Consanguineous marriage are acceptable in some cultures and in breeding will increase the disease expression of a particular genetic disease. We are investigating the role of parental consanguinity and the risk of epilepsy among siblings and children of probands with epilepsy.

Three hundred and sixteen patients with epilepsy who were Malaysians of Indian origin attending the University Malaya Medical Centre and Kuala Lumpur Hospital were interviewed. The family tree of the first degree relatives with history of epilepsy was constructed. History of single seizures was excluded. The mean age of the probands was 32 years. The age of onset of epilepsy was 19 years and the duration of epilepsy was 13 years. There was equal proportion of male and females. The probands had generalized tonic-clonic seizure (78%), complex partial seizure (12%) and loss of consciousness (7%). The mean seizure frequency was 8 per year. The seizures were classified as idiopathic (28%), cryptogenic (47%) and remote symptomatic (25%).

The probands had a mean of 3.7 siblings and 0.8 children. The mean age of the probands' sibling was 29 years, and age of the children was 4.4 years. Nineteen percent of the probands had a family history of epilepsy in first-degree relatives. These occurred among their siblings (12%), parents (4%), and children (2%). The lifetime prevalence of epilepsy among the sibling was 4.2% (N=47/1119); 4.1% (N=22/632) for the parents, and 2.9% (N=7/240) for the children. Majority (85%, n=22) of the proband's parents with epilepsy were fathers.

Parental consanguineous marriage was 29.5%. There was no difference in the demographics, seizure semiology and classification between the probands with consanguineous and non-consanguineous parental marriage. For the idiopathic and cryptogenic group, there was significantly higher rate of epilepsy among family members with consanguineous as compared to non-consanguineous parental marriage. For the idiopathic epilepsy group, the rate of epilepsy with consanguineous parental marriage was 9.8% (n=12/123) as compared to 3.7% with non-consanguineous marriage (n=15/4.3; p=0.02, RR=2.5, 95% CI: 1.2-5.2). For the cryptogenic epilepsy group, the rate of epilepsy with consanguineous parental marriage was 13.3% (n=28/209) as compared to 4% for non-consanguineous marriage (n=24/586; p<0.001; RR=3.0, 95% CI: 1.8-5.1). In the idiopathic epilepsy group, the rate of epilepsy among siblings of probands was significantly higher with parental consanguineous marriage (p=0.001, RR=5.3, 95% CI: 1.8-15.3). In the cryptogenic epilepsy group, the rate of epilepsy was significantly higher both the siblings (p=0.04; RR=2.4, 95% CI: 1.4-4.9) and children (p=0.000; RR = 8.5, 95% CI: 2.5-28.8) with parental consanguineous marriage. The relative risk of epilepsy for the siblings of idiopathic and cryptogenic epilepsy groups with parental consanguineous marriage was 3.1 (95% CI: 1.7-5.6). It was 2.8 (95% CI: 1.9-4.3, P<0.001) for their first-degree relatives. In idiopathic epilepsy group, there was higher risk of epilepsy siblings among those with younger age of onset of epilepsy (p<0.001).

In conclusion, the study shows an increased risk for epilepsy among siblings of patients with idiopathic and cryptogenic epilepsy that has parental consanguineous marriage. The risk of epilepsy in the children of those with cryptogenic epilepsy was also increased.

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