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Cytogenetic analysis in young people with Epilepsy disorder- A preliminary investigation

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ABSTRACT

Epilepsy is one of the most common neurological diseases worldwide. The present study was carried out to determine the chromosomal aberrations in peripheral blood samples of 20 patients with epileptic seizures as confirmed by their Electroencephalogram (EEG) reports. Subjects included for the study included 10 patients below the age group of 20 and 10 patients above the age group of 20. The majority of aberrations were mostly observed in patients with age group of ≥20 yrs old.

Key words: Epilepsy, Neurological disorder, Chromosome aberrations

INTRODUCTION

Epilepsy is a neurological disorder that affects people all over the world. It is characterized by a tendency to recurrent seizures and is defined by two or more unprovoked seizures. Research on epilepsy conducted worldwide estimated that it has a mean prevalence of approximately 8.2 per 1000 of the total population (Brodie and Schacther, 2001). Globally 50 million people suffer from epilepsy which is the most common neurological disorder affecting children in the developing world (Pal *et al*., 1998). Studies in developed countries suggest that the incidence of epilepsy is around 50 per 100,000 of the general population, where as in developing countries it is around 100 per 100,000 (WHO, 2001). The occurrence of epilepsy has been assessed in several populations worldwide (Annegers, 2004; Forsgren *et al*., 1996; Haerer *et al*., 1986; Hart *et al*., 1990; Hauser *et al*.,1991, 1993,1998; Juul-Jensen and Ipsen,1975; Sidenvall *et al*., 1996; Wallace *et al*.,1998). The rate of incidence of epilepsy tends to be high in early child hood (200 per 100,000 person-years), low (25- 40 per 100,000 person-years) between 20 and 50 years of age, and high after 50 years of age (Annegers, 2004; Forsgren *et al.,*1996; Hauser *et al.,*1993; Wallace *et al.,*1998). The overall prevalence proportion of epilepsy has been estimated to be 0.5 - 0.9% (Annegers, 2004; Forsgren *et al*.,1996; Haerer

et al.,1986; Hart *et al*.,1990; Hauser *et al*.,1991,1998; Juul-Jensen and Ipsen,1975; Sidenvall *et al*.,1996). About 6% of patients suffering from epilepsy with mental retardation carry chromosome aberrations (Singh *et al*., 2002).

MATERIALS AND METHODS

A total of 20 young patients with epilepsy were selected for this study using electroencephalogram (EEG) reports. The objectives of this study were explained to patients and their informed consent was obtained before including them for this study. The EEG is the depiction of the electrical activity occurring at the surface of the brain. This activity appears on the screen of the EEG machine as waveforms of varying frequency and amplitude measured in voltage (specifically microvoltage). The intravenous blood was collected aseptically using heparin from 20 patients suspected for seizure disorder. The patients were classified into two groups based on their age (Group I <20 yrs old and Group II ≥ 20 yrs old) to check for manifestation of any age-related changes in such patients. Age is a variable which is an important determinant for epilepsy risk. Age, as a surrogate of brain maturation, is a determinant of the specific characteristics of the seizure disorder in those with epilepsy, and age-related changes in these manifestations can be identified (Hauser,1992). Each group thus consisted of 10 patients.

Chromosomal aberration analysis was carried out by following standard procedure (Hoyos *et al*., 1996). Briefly, 0.5 ml of whole blood was added to 5.0 ml RPMI 1640 medium (Hyclone, USA), supplemented with 20% fetal bovine serum (PAA Laboratories, Austria), 2mM L-glutamine (Himedia, India), 1% streptomycin-penicillin antibiotic (Himedia, India) and 0.2 ml of Gibco™ phytohemagglutinin (ThermoFischer Scientific, India).

The mixture was incubated at 37°C for 72 hours. After 71 hours, the cells were treated with 0.01% Colchicine (Himedia, India) to arrest cells in mitosis. Lymphocytes were harvested upon the completion of 72 hours by centrifuging the cells at 1800 rpm for 7 minutes. About 6mL of pre-warmed (37°C) hypotonic solution (KCL 0.075 M) was added and left aside for 20 minutes at room temperature. After removing the hypotonic solution by centrifugation, the cells were fixed in Carnoy's fixative. Slides were prepared and stained in 2% Giemsa stain. For the chromosomal aberration analysis, 100 well spread metaphase plates were examined per subject under a microscope (100X) to identify numerical and structural chromosomal aberrations (Hoyos *et al*., 1996).

RESULTS

Table 1 shows the physical characteristics and chromosomal aberrations observed in the patients of the present study. Patients of both age groups showed both structural and numerical aberrations in different chromosomes. But the frequency was higher in Group II patients. Structural aberrations included deletions in long and short arms of chromosomes (5p-,7p-,14q-,15q-) and satellite structures in 13, 15 and 22nd chromosomes. Numerical aberrations such as trisomies observed for chromosomes 13 and 21.

In the present study almost all the patients exhibited tonic-clonic type of seizures. During the clonic phase of the seizures, the EEG derived from subdural electrodes overlying the motor strip always shows a polyspike wave pattern.

DISCUSSION

Epilepsy is the most common and challenging neurological disorder. This chronic disorder affects a patients' life by limiting his / her social, physical and emotional functions resulting in a poor quality of life. Improving an epileptic's Heath Related Quality of Life (HRQoL) is recognized as an essential component of the management of patients with epilepsy (Jacoby and Faker 2008, Privitera and Ficker , 2004). In the present study almost all the patients exhibited tonic-clonic type of seizures. When seizures occur during the childhood or in the third decade of life, generalized tonic-clonic are the most common together with partial simplex or partial complex seizures, but myoclonic, atonic and absence with tonic seizures have been reported (Singh *et al.,*2002).

An important application of EEGs is for the study of epileptic patients, in which deviations from the "normal" patterns help to classify epilepsies and eventually to localize the epileptic focus. Focal clonic seizures have been defined as series of myoclonic contractions occurring at regular intervals, typically in the range of 0.5± 5 Hz (Hamer *et al.,* 1999).

Table 1: Patients' health status and chromosome aberrations

Case. No	Gender/ age	Type of Seizure	Complaints	Life style factors	Chromosome aberrations
N001	15/F	Tonic-Clonic	Persistent cough Headache and tiredness	-	46, XX
N002	30/M	Tonic- Clonic	Wheezing trouble, Joint pain and severe headache	-	46, XY (5p-)
N003	28/F	Tonic- Clonic	-	-	46,XX
N004	22/M	Tonic	Headache and tiredness	-	46, XY
N005	17/F	Tonic- Clonic	Speech problem, Severing, Numbness Fearing and sleeping disturbance	-	46,XX
N006	14/M	Tonic	-	-	46,XY
N007	29/M	Tonic- Clonic	-	-	46, XY (7p-)
N008	16/F	Tonic-clonic	High Blood pressure, persistent cough and Joint pain	-	46, XX
N009	27/F	Tonic-clonic	Wheezing trouble and persistent cough	-	46, XX
N010	17/F	Tonic-clonic	-	-	46, XX
N011	14/M	Tonic-clonic	Spinal cord pain and Joint pain	-	46, XY (7p-)
N012	13/F	Tonic-clonic	-	-	46, XX
N013	20/M	Tonic-clonic	Unconsciousness	-	47, XY (5p-, $13S^+$ and $22S^+$), trisomy 21
N014	25/M	Tonic-clonic	Unconsciousness', Headache, Joint pain and weight loss	-	46, XY
N015	13/F	Tonic -clonic	Joint pain and Headache	-	46, XX
N016	22/M	Tonic clonic	Headache, unconsciousness	-	47, XY(14q-) trisomy 13
N017	24/ F	Tonic clonic	Headache	-	46, XX (14q-)
N018	15/ M	Tonic clonic	-	-	46, XY (15q-)
N019	22/M	Tonic clonic	Head ache and unconsciousness	-	46, XY
N020	18/M	Tonic clonic	-	-	47, XY ($15S^+$, $22S^+$) trisomy 21

Focal clonic seizures are always associated with a Polyspike wave pattern in the EEG of the primary motor area (frequency range 1.6±3.4 Hz). The clonic phase started at a frequency between 1.9 – 3.4 Hz in the present study of patients. The muscular contractions of the clonic phase are a response to brain activity that can only be established when brain oscillations are slow enough to be followed by the muscles. In the present study both structural and numerical chromosomal aberrations were observed in patients.

Structural chromosome aberrations present included deletions in chromosomes 5, 7, 14, 15, and satellite

structures in chromosomes 13, 15, and 22. Seizures onset ranging from neonatal period to 7 years are reported in patients affected with deletion of the long arm of chromosome 7. Febrile, generalized, myoclonic and combination of afebrile and febrile seizures are described in these cases. The only anomaly of chromosome 14 with a striking association with epilepsy is the ring 14. Numerous cases are reported, some of which are familial (Singh *et al.,* 2002). Recently reported is a syndrome due to 15q13.3 microdeletion associated with mental retardation, developmental delay and seizures. In these patients, seizures were of various types: myoclonic seizures, absence seizures, tonic-clonic seizures, intractable epilepsy (Sharp *et al.,* 2008). Epilepsy has been an uncommon manifestation associated with 22q11 deletion. It is present in less than 5% of the patients (Roubertie *et al*., 2001)

In the present study numerical chromosome aberrations recorded included trisomy in 13 and 21st chromosomes in a mosaic manner along with structural chromosome aberrations in both groups of patients. In trisomy 13 or Patau syndrome, seizures are reported rarely even if a variety of developmental abnormalities of the brain are present: holoprosencephaly (60-80% of cases), cerebellar dysplastic changes, olfactory aplasia, hippocampal hypoplasia and callosal agenesis. Epilepsy occurs in 8% of individuals with Down syndrome (DS). Age of seizure onset is bimodal: 40% occurs before 1 year of age and 40% occur in the third decade of life (Roizen and Patterson, 2003). The increased seizure susceptibility has been attributed to inherent structural anomalies of the brain such as fewer inhibitory interneurons, decreased neuronal density, abnormal neuronal lamination, persistence of dendrites with foetal morphology or primitive synaptic profiles (Stafstrom *et al*., 1991).

In conclusion, this preliminary study provides valuable information on different types of aberrant karyotypes in epileptic patients of different young age groups in the population studied. Further studies with a large sample size and better classification are needed to delineate the clinical features of epileptic seizures and to understand the mechanisms of epilepsy associated with chromosomal abnormalities.

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Conflict of Interests
No funds were received for this study. Authors do not have any conflicting interests.

REFERENCES

Annegers FJ, Epilepsy. In: Nelson LM, Tanner CM, Van Den Eeden SK, McGuire VM. (Eds.), Neuro epidemiology. From Principles to Practice. Oxford University Press, New York, 2004; pp. 303-318.

Brodie MJ, Schachter SC. Fast Facts. Epilepsy. 2nd ed. Health Press, 82, Oxford 2001.

Epilepsy: Aetiology, epidemiology and prognosis. Fact sheet No.168. Geneva: World Health Organization; 2001.

Forsgren L, Bucht G, Eriksson S, Bergmark L (1996). Inciden and clinical characterization of unprovoked seizures in adults: prospective population-based study. *Epilepsia* 37, 224-229.

Haerer AF, Anderson DW, Schoenberg BS (1986). Prevalence and clinical features of epilepsy in a biracial United States population. *Epilepsia* 27: 66-75.

Hamer HM *et al* (1999) Symptomatology of epileptic seizures in the first three years of life. *Epilepsia* 40: 837-44.

Hart YM, Sander JW, Johnson AL, Shorvon SD (1990) National General Practice Study of Epilepsy: recurrence after a first seizure. *Lancet* 336:1271-1274.

Hauser WA *et al*. (1998). Risk of recurrent seizures after two unprovoked seizures. *N. Engl. J. Med* 338: 429-434.

Hauser WA, Annegers JF, Kurland LT (1991) Prevalence of Epilepsy in Rochester, Minnesota: 1940—1980. *Epilepsia* 32: 429 - 445.

Hauser WA (1992). Seizure disorders: the changes with age. *Epilepsia* 33 Supple 4: S6-14.

Hauser WA, Annegers JF, Kurland LT (1993) Incidence of epilepsy and unprovoked seizures in Rochester, Minnesota: 1935—1984. *Epilepsia*; 34: 453- 468.

Hoyos LS *et al*. (1996) Cytogenetic monitoring of farmers exposed to pesticides in Colombia. *Environ Health Perspect* 104 (3) 535 – 538.

Jacoby A, Baker GA (2008) Quality-of-life trajectories in epilepsy: a review of the literature. *Epilepsy Behav* 12: 557-71.

Juul-Jensen P, Ipsen J (1975) Prevalence and incidence of epilepsy in Greater Aarhus. *Ugeskr Laeger* 137, 2380 - 2388.

Pal D, Das T, Sengupta S (1998) Comparison of key informant and survey Methods for ascertainment of

childhood epilepsy in West Bengal, India. *Int J Epidemiol,* 27: 672–6.

Privitera M, Ficker DM (2004) Assessment of adverse events and quality of life in epilepsy: design of a new community-based trial. *Epilepsy Behav* 5: 841-6.

Roizen NJ, Patterson D (2003). Down's syndrome**.** *Lancet* 361:1281-1289.

Roubertie A *et al*. (2001) Neurological presentation of three patients with 22q11 deletion (CATCH 22 syndrome)**.** *Brain Dev*23:810-814.

Sharp AJ *et al*. (2008) A recurrent 15q13.3 micro-deletion syndrome associated with mental retardation and seizures**.** *Nature Genetics* 40:322-328.

Sidenvall R, Forsgren L, Heijbel J (1996) Prevalence and characteristics of epilepsy in children in Northern Sweden. *Seizure* 5: 139 - 146.

Singh R *et al*. (2002) Chromosomal abnormalities and epilepsy : a review clinicians and gene hunters, *Epilepsia* 43: 127 – 140.

Stafstrom CE *et al*. (1991) Seizures in children with Down syndrome: etiology, characteristic and outcome**.** *Dev Med Child Neurol* 33:191-200.

Wallace H, Shorvon S, Tallis R (1998) Age-specific incidence and prevalence rates of treated epilepsy in an unselected population of 2,052,922 and age - specific fertility rates of women with epilepsy. *Lancet* 19 – 26 (352), 1970-1973.