Epilepsia, 31(6):718–723, 1990
Raven Press, Ltd., New York

Epidemiology of Epilepsy in Guaymi Indians from Bocas del Toro Province, Republic of Panama

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Summary: This cross-sectional study was conducted to describe the epidemiology of epilepsy in Guaymi Indians residing in Changuinola, a small town on Panama's Caribbean coast near Costa Rica. We randomly selected households and attempted to enroll all residents aged ≤1 year; 337 eligible subjects agreed to participate (93% response rate). We administered a standard neurologic disease screening examination to all subjects and, if any abnormality was found, we administered a standard neurologic evaluation. We detected 19 cases of active epilepsy; the mean age at onset was 12 years, and generalized tonic-clonic seizures were the most common diagnosis (10 of 19, 53%). The prevalence of active epilepsy among Caribbean coastal Guaymi (57/1000) is considerably greater than that in lower class Panama City populations (22/1000) or in other parts of the world. To identify risk factors for epilepsy, we collected epidemiologic data and serum (for *Cysticercus* antibody) from subjects with active epilepsy and from 44 age/sex-matched controls. Significantly more cases (47%) than controls (6%) had other family members with epilepsy (relative risk, RR = 14); 44% of cases and 13% of controls reported a history of febrile seizures during childhood (RR = 6). **Key Words:** Epilepsy—Epidemiology—Prevalence—Amerinds; Panama—Latin America.

Numerous studies have shown that the prevalence of epilepsy is considerably higher in developing than in industrialized countries (reviewed in Osuntokun et al., 1987). This disparity may be partly explained by differences in diagnostic criteria and study design, but other factors unique to developing countries may also be important. These include inadequate public health services, particularly obstetric care and vaccination programs, exposure to infectious agents such as *Taenia solium* (*Cysticercus*), and head injury.

The Republic of Panama is similar to many Caribbean basin countries. The capital is a modern metropolitan city and international financial center and the rest of the country's predominantly rural population practices agriculture. In contrast to many other countries in the region, Panama has a well-organized public health system. A previous study in Panama City documented a high prevalence of active epilepsy (22/1,000) (Gracia et al., 1988). During studies of human T-cell lymphotropic virus (HTLV) among Guaymi Indians from Bocas del Toro province (where HTLV seroprevalence is ~9%), we found an unusually high occurrence of epilepsy (not associated with HTLV infection). We therefore conducted the present study to determine the prevalence of historic and active epilepsy in Guaymi Indians and to identify associated risk factors.

Received July 1989; revision accepted November 1989.

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MATERIALS AND METHODS

Study population

Guaymi Indians

Guaymi Indians inhabit isolated segments of Chiriqui, Veraguas, and Bocas del Toro provinces, Republic of Panama, and portions of Puntarenas province, Costa Rica. Present-day Guaymi proba-

bly represent one or more Indian groups who retreated to the mountains in this region in response to Spanish colonization. Relative isolation has persisted for ~300 years, and the Guaymi today are still largely unadmixed with people of European or African descent (Barrantes et al., 1982). Acculturation is occurring, however, and one manifestation involves immigration to urban areas where salaried jobs are available at banana plantations. Entire nuclear families migrate together and live in housing areas provided by the plantation. In addition, amenities such as education and health services are provided for workers and their families.

Population survey

Guaymi Indians, ≥1 year old, who resided in banana plantation housing areas in Changuinola, Bocas del Toro province, in April, 1988 comprised the study population. We selected homes randomly from census bureau maps according to sample size calculations for the HTLV study. Survey teams, composed of epidemiology technicians from the Gorgas Memorial Laboratory and a Guaymi Indian labor union representative–translator visited each house, explained the purpose of the study, tabulated all residents, and obtained informed consent. Competent adults were interviewed (when necessary through the translator) for basic epidemiologic data and to detail familial relationships. Consenting participants also had 10 ml venous blood collected; specimens were separated, aliquoted, and frozen on the evening of collection.

The Panamanian Census Bureau estimated 1,498 Guaymi lived in urban Changuinola; 395 Guaymi Indians (26% of the estimated population) resided in the selected homes, 366 (93%) were contacted for the study, and 337 were aged ≥1 year. The 29 Indians who did not participate could not be located at the time of the survey; no subject refused to participate.

Neurologic disease survey

A two-phase study design was used to identify neurologic disease. The first phase screened the entire study population, and the second phase evaluated subjects detected by the screen as possibly having neurologic disease. The standard World Health Organization neurologic screening examination for use in developing countries was administered by specially trained epidemiology technicians to all subjects aged ≥1 year (WHO, 1981; Schoenberg, 1987). The screen combined an interview and physical examination and was designed to detect possible epilepsy, peripheral neuropathies, extrapyramidal disorders, and cerebrovascular pathology. All individuals with any abnormality noted on the screening examination were further evaluated 1 or 2 days later by a study neurologist who determined a differential diagnosis.

We defined a seizure as an abrupt change in state of consciousness, an alteration of perception of the environment, or an involuntary alteration of the individual's responses to the environment. We defined epilepsy as a condition in which seizures tended to occur chronically. Active cases of epilepsy were defined as at least two afebrile seizures within the last 2 years; at least one must have been seen by a reliable witness and must not have been secondary to alcohol or drug consumption (Gastaut et al., 1980). Study neurologists classified each case of epilepsy using criteria of the International League Against Epilepsy (Merlis, 1970). Clinical classification was based on unequivocal manifestations and symptoms, and subjects with possible or borderline epilepsy were excluded.

Case control study of epilepsy

Approximately 6 weeks later, we conducted a case control study to evaluate possible risk factors for epilepsy. Subjects diagnosed as having prevalent epilepsy in phase 2 were cases, and we used lists of screen-normal subjects to select two controls per case randomly, matched by sex and 5-year age group. Cases were evaluated a second time by a neurologist to confirm diagnosis and to ascertain whether epilepsy was active. These evaluations were made blinded as to the previous phase 2 evaluation. Controls had a detailed neurologic examination by a neurologist to ascertain that they did not have epilepsy. Cases and controls were administered a standardized questionnaire in Spanish to ascertain possible risk factors.

Laboratory methods

Marianna Wilson, Division of Parasitic Diseases, Centers for Disease Control (Atlanta, GA) tested sera for *Taenia solium* (cysticercosis) antibody by means of an immunoblot assay (Tsang et al., 1989). Positivity in this assay is based on recognition of one or more cysticercus-specific glycoprotein bands in a purified antigen fraction.

RESULTS

Neurologic disease survey

One hundred-six (29%) of 337 Guaymi Indians were detected in the screening exam as possibly having neurologic disease; 101 (95%) were reexamined by a study neurologist, and 32 (32%) had neurologic abnormalities documented (Table 1); six other subjects gave a history of syncope or collapse, and four had musculoskeletal pathology

TABLE 1. *Neurologic disorders diagnosed after screening examination of Guaymi Indians*

ICD 9 Code 345.0–345.9	All forms of epilepsy	n = 30
345.1	Generalized convulsive epilepsy	13
345.9	Epilepsy not otherwise specified	11
345.0	Generalized nonconvulsive epilepsy	3
345.4	Partial epilepsy with impairment of consciousness	2
345.5	Partial epilepsy without impairment of consciousness	1
3469	Migraine	1
3569	Hereditary and idiopathic neuropathies	1

which was manifested during the screening examination as gait disturbance. Epilepsy was the most common neurologic disease diagnosed, occurring in 30 (9.0%) of 332 subjects.

Case control study

Twenty-five (83%) of 30 subjects diagnosed with epilepsy after the screening examination and 44 (67%) of the selected controls were available for the case control study; the remainder could not be located. Nineteen (76%) of the 25 epilepsy cases were active, so that the estimated prevalence of epilepsy among Guaymi Indians aged ≥1 year was 19 of 332 (5.7%). Only one subject (with active epilepsy) had a prior diagnosis of epilepsy, and he was not receiving antiepileptic drug (AED) therapy. The remainder of the analysis is restricted to active cases.

Most patients were classified as generalized tonic clonic epilepsy (53%) or complex partial epilepsy (26%) (Table 2). There were 10 males and 9 females. The mean age was 23.5 years (range 1–51 years, SD 15.5 years); the average age at onset was 11.9 years (range 1 month to 41 years, SD 12.0). All 19 patients with epilepsy had normal neurologic examinations. No clinical evidence of cerebrovascular disease or brain tumor was observed. Similarly, there was no evidence that head trauma or perinatal brain injury (both defined as loss of consciousness >30 min) had occurred in patients or controls.

To estimate the risk of epilepsy associated with selected exposures, we calculated odds ratios, as approximations of relative risks (RR) (Table 3). History of epilepsy among first-degree family members (parents, siblings, children) was the most significant risk factor (RR = 13.9) and a history of febrile seizures before age 7 years was also significantly associated with active disease (RR = 5.6). In addition, 5 (28%) of 18 patients but none of 30 controls were positive for both risk factors; i.e., a reported family history of epilepsy and a history of febrile seizure before age 7 years ($p < 0.005$, Fisher's exact test). All serum specimens were unequivocally negative for *Cysticercus* antibody.

We were able to construct detailed family trees for 13 subjects with active epilepsy (Fig. 1). The 13 patients came from seven families and nine of the cases of epilepsy occurred in three families (totaling 18 members), so that 50% of family members were diagnosed as having active epilepsy. In four families, only one case was diagnosed, but these families were primarily composed of young children who may later develop disease manifestations. Finally, we could not detect differences in current socioeconomic status or utilization of health care between epilepsy cases (or case families) and controls, but the population was selected based on occupation and the sample size was small.

TABLE 2. *Characteristics of Guaymi Indians with active epilepsy*

Diagnosis	n (%)	Age at onset[a]
Generalized epilepsy	12 (64)	1 mo–31 yr (9)
Tonic clonic epilepsy	10 (53)	
Absence epilepsy	2 (11)	
Partial epilepsy	6 (31)	8 mo–41 yr (19)
Simple partial epilepsy	1 (5)	
Complex partial epilepsy	5 (26)	
Epilepsy not classified	1 (5)	1 yr

[a] Age at onset shown as age range and average.

DISCUSSION

This study showed a prevalence of 57 per 1,000 Guaymi Indians living on banana plantations in Changuinola had active epilepsy. The study was population-based and used standardized screening instruments administered by trained epidemiology technicians, standard case definitions, and standard diagnostic criteria. A study using the same methodology documented the prevalence of active epilepsy in Panama City as 22 in 1,000 (Gracia et al., 1988),

TABLE 3. *Associations between epilepsy and various risk factors in Guaymi Indians*

Risk factor	Cases n (%)[a]	Controls n (%)[a]	RR	95% CI
Epilepsy in other family members	9/19 (47)	2/33 (6)	13.9	2.2–71.5
Febrile seizure before age 7 years	8/18 (44)	4/32 (13)	5.6	1.2–29.1
Head trauma	7/19 (37)	7/34 (21)	2.3	0.5–9.4
History of central nervous system disease	0/16 —	0/29 —	—	—
Alcohol drinker	11/19 (58)	17/35 (49)	1.5	0.4–5.2
HTLV seropositive	4/19 (21)	3/36 (8)	2.9	0.5–19.5
HBsAg seropositive	3/19 (16)	5/36 (14)	1.2	0.2–6.7

RR, relative risk approximated by the odds ratio; CI, confidence interval.

[a] Denominators vary because of unknowns.

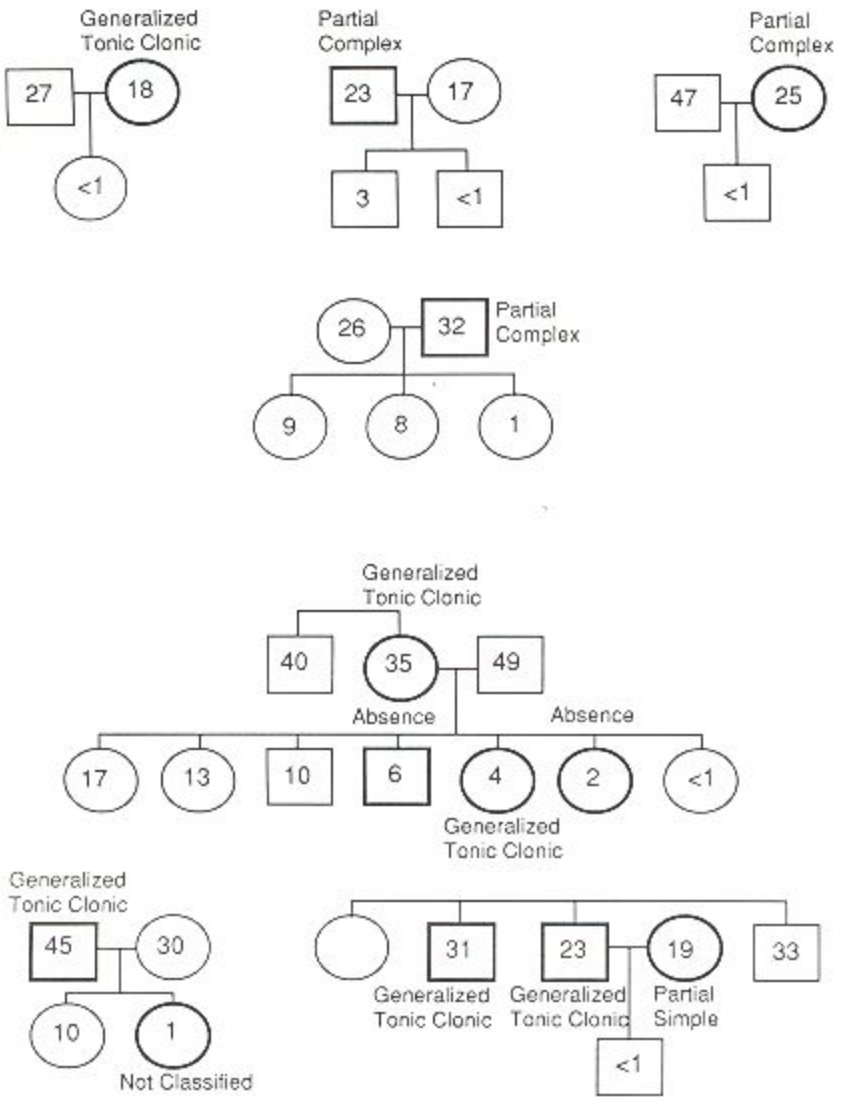

FIG. 1. Genetic linkages of Guaymi Indian epilepsy cases. Standard genetic symbols were used: Circles denote female, squares denote male; age (in years) is written inside the symbol; diagnoses appear proximal to a darkened symbol. All other patients were examined and were neurologically normal.

which is similar to the general range between 4 and 49 in 1,000 reported from developing countries (Gomez et al., 1978; Chiofalo et al., 1979; Osuntokun et al., 1987). In contrast, the prevalence of epilepsy in industrialized countries varies between 4 and 7 in 1,000 (Hauser and Kurland, 1975; Kurtzke and Kurland, 1983). Although it is impossible to compare studies directly because of variation in study design (referent populations and case detection) and case definition, the prevalence of active epilepsy was considerably greater among Guaymi Indians than has been documented by other studies.

The most important risk factor for epilepsy among Guaymi Indians was a history of epilepsy among other family members (RR = 14). We obtained data used to derive RR estimates by querying subjects as to whether first-degree blood relatives had epilepsy and were able to validate responses by reviewing patients with active epilepsy in living units. Febrile convulsions are also known to be associated with a three- to sixfold increased risk for epilepsy, as we found in this study (Nelson and Ellenberg, 1978; Annegers et al., 1979). Our study found high rates of febrile seizures in both patients (44%) and controls (13%), which is similar to studies in Africa (Ogunniyi et al., 1987; Osuntokun et al., 1987). The risk of febrile seizure among Guaymi and among Africans is considerably higher than one estimate indicating that 2.3–4.6% of the normal white U.S. population have suffered febrile seizures (Leviton and Cowan, 1981).

Epileptiform seizures are the most common sign of neurocysticercosis caused by the larval stages of *Taenia solium*, the pork tapeworm. Although this cestode is endemic throughout Central America it has been reported rarely in Panama (Gracia et al., in press). The absence of cysticercosis antibody in patients and controls suggests that neurocysticercosis was not the cause of epilepsy in the Guaymi population. The cysticercosis immunoblot assay used in

this study was previously shown to be 98% sensitive for serologic diagnosis of >130 patients with surgically confirmed neurocysticercosis (Tsang et al., 1989).

High rates of epilepsy in underdeveloped countries may reflect lack of access to prenatal, obstetric, or postpartum medical care; a high prevalence of both maternal and pediatric malnutrition; or a high incidence of childhood infections. A well-organized rural public health program exists in Changuinola, however, where our population resided, and the maternal and child health component appears to have had good penetration into the Guaymi Indian community. The mothers of most children in both case and control households received prenatal and obstetric care, virtually all children had received all recommended vaccinations, and no child had clinical malnutrition. Bringing optimal public health to high-risk target populations entails many problems however; e.g., only 1 of the 19 patients with active epilepsy we detected had been previously diagnosed (and was not receiving AEDs). Guaymi Indians apparently do not perceive epilepsy as a severe problem amenable to treatment. Even though there were no obvious differences between patients and controls in utilization of health services, a uniform low level of such resources may contribute to an overall elevated risk of disease.

We classified type of epilepsy based on descriptions of seizures by patients and witnesses. Generalized tonic-clonic seizures were the most common manifestation (53% of cases), followed by complex partial seizures (26%). It is difficult to compare these figures critically with reports in the literature because various classification systems have been used. Indeed, some studies have shown a similar distribution (Sato, 1964; Gudmundsson, 1966), whereas others have reported that partial epilepsy is more common (Gastaud et al., 1975; Hauser and Kurland, 1975; Joshi et al., 1977; Gomez et al., 1978).

To interpret our findings, it is necessary to appreciate problems inherent in studies of diseases like epilepsy among populations such as the Guaymi Indians for whom cultural concepts such as time and perception of health are not amenable to standardized interviews. The diagnosis of epilepsy is clinical and relies on accurate analysis of contemporary eyewitness accounts of events. Seizure episodes can be dramatic, with the body undergoing a series of violent spasms, or they can be subtle, manifesting as simple fluttering of the eyelids. Responses to questions about seizures may depend on the exact terminology used in different population groups (Anderson et al., 1988). Our interviews were not conducted firsthand in the subjects' native language; although most subjects spoke Spanish, interpreters were used occasionally in interviews. We attempted to overcome problems in translation by having study neurologists conduct final definitive examinations and supervise interviews, by carefully explaining the purpose of the study and discussing epilepsy with the translators, and by requiring subjects (or witnesses) to demonstrate or recapitulate seizure episodes. If any reasonable doubt existed, diagnoses were discarded. Thus, we believe we have underestimated the true occurrence of epilepsy in this population.

Acknowledgment: We thank Juan Ramon Arosemena, Marina Cuevas, Mariana Garcia, Itzy Gonzalez, Cidia Guillen, Bonnie de Moore, Vielka Pinzon, Layla de Perez, Maritza Ramos, Renata Rivas, and Denisse Saez of the *Gorgas Memorial Laboratory;* Pablo Beitia, Mariela de Diaz, and Waldemar Oliveros of *Integrated Health System, Changuinola;* Gilda Ayala, Pablo Rayo, Juan Becker, and Elia Sanchez of the *Sindicato de Trabajadores de la Chiriqui Land Company;* Ezequiel Jethmal and Ana Aguirre of the *Complejo Hospitalario Metropolitano–CSS;* and Marianna Wilson, John R. Cutler, Robert S. Janssen, and Edwin Trevathan of the *Centers for Disease Control.*

This work was conducted by the Gorgas Memorial Laboratory, Panama, and was supported in part by Contract No. NCI-CP-31015, the National Cancer Institute, National Institutes of Health.

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RÉSUMÉ

Cette étude transversale a été conduite avec l'intention de décrire l'épidémiologie de l'épilepsie chez les indiens guaymi de Panama, qui vivent sur la côte caraïbe près du Costa Rica. Nous avons choisi au hasard des familles, et nous avons essayé de faire porter notre enquête sur tous les membres de ces familles âgés d'un an ou plus; 337 sujets ont accepté de participer à cette enquête (97%). Tous les sujets ont passé un examen de détection, et les cas repérés ont été examinés par les neurologues. Nos avons trouvé 19 cas d'épilepsie active. L'âge moyen de début de la maladie est 13 ans. Le diagnostic le plus fréquemment rencontré a été l'épilepsie tonico-clonique généralisée (10/19, 53%). La prévalence de l'épilepsie active parmi les guaymi de la côte caraïbe (57/1000) est nettemente supérieure à celle de la population pauvre de la ville de Panama (22/1000) et à celle de toute autre population étudiée. Pour identifier les facteurs de risque nous avons collecté l'information épidémiologique et recueilli de sérum (anticorps anti-Cysticercus) des sujets atteints d'épilepsie et nous avons effectué 44 contrôles dans les mêmes conditions d'âge et de sexe. Il y avait significativement plus d'antécédents d'épilepsie familiale (RR = 14) chez les malades (47%) que chez les sujets contrôlés (6%); 44% de épileptiques et 13% des sujets contrôlés ont fait état de convulsions fébriles dans l'enfance.

(Translation supplied by authors)

RESUMEN

Este estudio transversal fue dirigido para documentar la prevalencia de epilepsia en los indios guaymi de Changuinola en la costa Caribe de Panamá, cerca de Costa Rica. Seleccionamos residentes al azar e intentamos captar todos de un año o más, de los cuales 337 personas elegibles estuvieron de acuerdo en participar (93% respuestas evaluadas). A todos los participantes se les aplicó el formulario de la Organización Mundial de la Salud para enfermedades neurológicas, si se encontró alguna anormalidad, el paciente fue examinado por el neurológo en detalle. Detectamos 19 casos de epilepsia activa; la edad promedio encontrada fue de 13 años y el diagnóstico más común fue convulsiones tónico clónico generalizadas (10/19, 53%). La prevalencia activa de epilepsia entre los Guaymi de la costa Caribeña (57/1000) es considerablemente más allá que en la clase social baja de la población en la ciudad de Panamá (22/1000) o de otras partes del mundo. Con el propósito de identificar factores de riesgo para epilepsia, obtuvimos información y sueros (para anticuerpos de cisticercosis) de los casos con epilepsia y de 44 controles apareados por edad y sexo. Significativamente más casos (47%) que controles (6%) tuvieron otros miembros de la familia con epilepsia (RR = 14); 44% de los casos y 13% de los controles indicaron una historia de convulsiciones febriles durante su niñez (RR = 6). Ningún otro factor de riesgo fue identificado.

(Translation supplied by authors)

ZUSAMMENFASSUNG

Um die Epilepsie-Epidemiologie der Guaymi Indianer in Changuinola, einer kleinen Stadt an der Panamaischen Karibikküste, zu erforschen, wurde diese Feldstudie durchgeführt. Wir suchten randomisierte Haushalte auf und versuchten alle Bewohner über 1 Jahr zu erfassen. 337 Personen waren einverstanden an der Studie teilzunehmen (93%). Routinemäßig wurde ein standartisierter neurologischer Fragebogen benutzt und bei Auffälligkeiten eine neurologische Untersuchung angeschlossen. Wir fanden 19 Fälle mit aktiver Epilepsie: Beginn im Mittel mit 12 jahren, meist tonischklonische Anfälle (53%). Die Prevalenz von Epilepsie beträgt somit bei karibischen Indianern 57/1,000 und ist damit beträchtlich höher als bei der Unterschicht in Panama City (22/1,000) oder anderen Erdteilen. Um die Risikofaktoren näher zu bestimmen, erfolgte die Sammlung epidemiologischer Daten von Seren zur Cysticercus-Antikörper-Bestimmung von 44 Anfallskranken und 4 alters- und geschlechtsgleichen Kontrollpersonen. Während die Kontrollpersonen nur in 6% Familienangehörige mit Epilepsie hatten, lag dieser Wert bei den Anfallskranken bei 47%. 44% der Anfallskranken hatten Fieberkrämpfe gehabt, dagegen nur 13% der Kontrollpersonen.

(C. G. Lipinski, *Heidelberg/Neckargemünd*)