

## SEROEPIDEMIOLOGICAL AND CLINICAL STUDY OF CHAGAS' DISEASE IN NICARAGUA (1)

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### SUMMARY

With the aim of determining the prevalence, immunological profile, and knowing the electrocardiographic alterations, a clinical and seroepidemiological study of Chagas' disease was performed in three rural settlements located at the North, East and West of Nicaragua.

Anti *T. cruzi* antibodies were searched by indirect immunofluorescence (IFI) and hemagglutination (IHA) in a total of 803 subjects. Seropositives and the same number of seronegatives, matched by age and sex, were included in a case-control design for the electrocardiographic assessment.

Antibody prevalence was 13.1, 4.3 and 3.2% in the respective settlements. In the first two the immunological profile corresponds to that of an endemic zone of long standing, where transmission has decreased, and in the third the pattern is of a zone under control.

Electrocardiographic changes compatible with Chagas' disease were found in seropositive individuals, but difference with control group was not statistically significant. It is concluded that the disease is endemic in the three settlements and the clinical aspect requires further evaluation, including additional cardiologic techniques.

**KEYWORDS:** . Chagas' disease; Chagasic cardiomyopathy; Seroepidemiology; Nicaragua.

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### INTRODUCTION

According to the 1991 WHO report on control of Chagas' disease <sup>17</sup> 16 to 18 millions persons are infected and 100 millions are at risk of acquiring the disease. This same report informs of an increase of disease transmission in recent years.

In Nicaragua, the first suspected cases of American trypanosomiasis were described in 1949. In 1965 URROZ & ESPINOZA <sup>16</sup> confirmed the existence of the disease in the Northern zone of the country and found *Rhodnius prolixus* as the primary vector and

*Triatoma dimidiata* as the secondary one. Afterwards, there have been studies demonstrating the existence of the epidemiological chain elements in various zones <sup>8,14</sup>, which indicates that this disease could be widely distributed in the country. However, the existing reports are not enough to fully assess the magnitude of the health problem that Chagas' disease poses for our country.

With the aim of advancing the knowledge of the situation of the disease, a clinico-epidemiologic survey

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has been carried out in three zones of Nicaragua: Northern (Somoto), Eastern (Masaya) and Western (Poneloya).

## MATERIALS AND METHODS

A total of 803 subjects from three rural communities located in different geographic zones of Nicaragua were studied. These communities were: Santa Rosa, Quebrada Honda and Poneloya (Fig. 1).

Santa Rosa is located at an altitude of 600 m in the department of Madriz in the Northern zone of the country. This is a mountainous region with tropical and mixed type forest. The settlement has 115 houses with 861 inhabitants, who live from agriculture, producing maize, sorghum and beans. Their dwellings are built with several kinds of materials: 1) mud-brick on a wooden structure and tile roof, 2) walls of sorghum canes and thatch roofing, and 3) a mixture of the above mentioned materials. All of the houses had earthen floors.

Quebrada Honda is in the Eastern region, in the municipality of Masaya. Its altitude is 300 m, and the vegetation consists of forests and shrubs, and the main crops are fruits. In this settlement there are 120 houses with a population of approximately 700 inhabitants. The houses are made of: 1) bricks with cement plastering and tile or galvanized sheet roof, 2) wooden

walls and tile or thatch roof, and 3) walls of canes and thatch roofing. All houses have earthen floors.

Poneloya is next to the Poneloya resort in the municipality of León. The community has 70 houses and 600 inhabitants and the ecological features are those of a dry zone in which the main culture has been cotton. Most of the houses have brick walls and galvanized sheet roof, with concrete lined floors.

An explanation on the nature and objectives of the study was given to the subjects and their verbal consent was obtained before the initiation of the study.

### Serological indicator:

Sampling was made by systematic random, selecting alternate houses. All the individuals present in the house at the time of the visit, and who provided a blood sample, were included in the study. In total, 803 subjects were studied, which represents 36.7% of the total population of the three areas. From each individual 50µl of blood were obtained by finger prick. The sample was preserved in collecting vials, containing 150µl of buffered glycerin, from the Serokit system (Biotica S.A.I., Argentina).

The blood samples were assayed, at the Microbiology laboratory of the Faculty of Medicine in León, by the indirect hemagglutination (IHA) and indirect immunofluorescent (IFI) tests, standardized in accordance with the Instituto de Investigación y Diagnóstico de la Enfermedad de Chagas "Dr. Mario Fatala Chabén", in Buenos Aires. The threshold positive titre was 1:32 for both tests, according to the international standardization for serodiagnosis of Chagas' disease<sup>4</sup>. Samples with discordant results in both tests were considered negatives.

Distribution of seropositivity was determined by age and sex. Associations between seropositivity and structural characteristics of the house were sought by the Chi-square test. A further analysis was made by combining the house variables into a complex index of housing condition, according to the BRONFMAN et al.<sup>2</sup> model. This index classifies the houses into three categories: bad, regular and good.

### Clinical indicator

A matched case-control design was followed to determine electrocardiographic abnormalities attribu-



Fig. 1 - Map of Nicaragua indicating the location of the three rural communities surveyed for Chagas' disease.

table to Chagas' disease. Cases were defined as seropositive individuals by both immunological tests. Seronegative subjects of the corresponding age and sex were chosen as controls.

The electrocardiograms were performed with a Fokuda apparatus with 12 leads, operating at a speed of 100mm/sec in children and 50mm/sec in adults, and at 0.5 volts. Reading of electrocardiograms was performed, being unaware of serological status, by a cardiologist from the Universidad Nacional Autónoma de Nicaragua, León, and by a specialist in chagasic cardiology from the Castex y Ramos Mejía Hospital, Buenos Aires. Statistical comparison between cases and controls was done by the Fisher's exact test.

## RESULTS

### 1. Serological indicator

An overall prevalence of 7.1% was found in the 803 examined sera. The prevalence by community was: 13.1% in Santa Rosa, 4.3% in Quebrada Honda and 3.2% in Poneloya. A significant difference in prevalences ( $p=0.000005$ ) was found between Santa Rosa and the other communities.

The immunological profile for Santa Rosa is characterized by a sustained rise from the first years of age, up to a maximum in the oldest group (Fig. 2). In Quebrada Honda the profile indicates an irregular, low grade transmission, still occurring in the less than five years old (3.1%), and with the highest rate (14.3%) in the over 50 age group.

The distribution of seropositives by housing condition is shown in Table 1. There were not significant

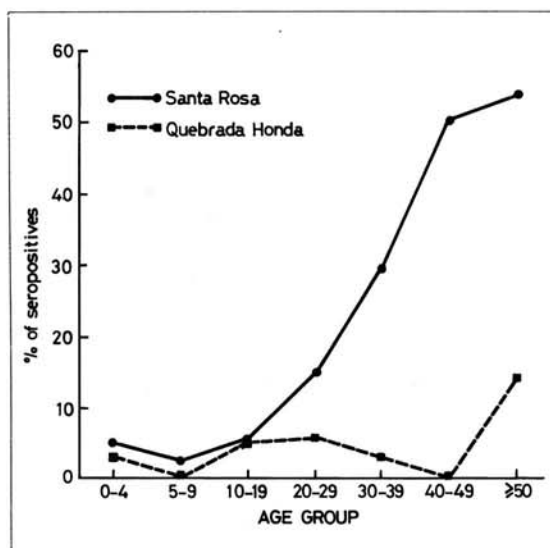


Fig. 2 - Seropositivity to *T. cruzi* by age group in the Santa Rosa and Quebrada Honda communities, Nicaragua.

differences between house condition and seropositivity in Santa Rosa and Quebrada Honda; but an apparent association between good housing and infection was found in Poneloya ( $p=0.0057$ ).

### 2. Clinical Indicator

Electrocardiographic abnormalities of atrio-ventricular block, sinus bradycardia and decreased R wave types, were found in 12 (38.7%) of 31 cases and in 10 (27%) of 37 controls, with an odds ratio of 1.5, in Santa Rosa; but the difference was not statistically significant (Table 2). In the distribution of electrocardiographic abnormalities in cases and controls by age group, the higher rates were found in the over 45 age

TABLE 1  
Relationship between seropositivity to *T. cruzi* and housing condition in three Nicaraguan communities, 1989-1992.

Housing condition	Community					
	Santa Rosa <sup>a</sup>		Quebrada Honda <sup>b</sup>		Poneloya <sup>c</sup>	
	No. of examined	Seropositives No. (%)	No. of examined	Seropositives No. (%)	No. of examined	Seropositives No. (%)
Bad	59	9 (15.3)	78	4 (5.1)	10	0 (0.0)
Regular	183	24 (13.1)	110	4 (3.6)	186	2 (1.1)
Good	3	0 (0.0)	33	0 (0.0)	83	7 (8.4)

a:  $p = 0.723$   
b:  $p = 0.417$   
c:  $p = 0.0057$

TABLE 2

Electrocardiographic abnormalities in cases and controls from two chagasic endemic zones of Nicaragua, 1989.

Zone 1 Santa Rosa (Somoto)

EKG	Cases (N=31)		No.	Controls (n=37)		p*
	No.	%		No.	%	
Sinus arrhythmia	0	0.0	1	2.7	NS	
First degree AV block	2	6.5	0	0.0	NS	
Sinus bradycardia	2	6.5	1	2.7	NS	
Decreased R wave	2	6.5	1	2.7	NS	
Decreased voltage	1	3.2	0	0.0	NS	
Supraventricular extrasystoles	1	3.2	0	0.0	NS	
Ventricular extrasystoles	0	0.0	2	5.4	NS	
Left anterior hemiblock	1	3.2	1	2.7	NS	
Right ventricle overload	1	2.7	0	0.0	NS	
Sinus tachycardia	0	0.0	1	2.7	NS	
Intra atrial conduction alterations	0	0.0	1	2.7	NS	
Anterior wall repolarization disturbs	2	6.5	2	5.4	NS	
Total	12	38.7	10	27.0	NS	

Zone 2: Quebrada Honda (Masaya)

EKG	Cases (n=8)		No.	Controls (n=7)		p*
	No.	%		No.	%	
Right bundle branch block	1	12.5	0	0.0	NS	
Supraventricular extrasystoles	0	0.0	1	14.2	NS	
Anterior wall repolarization disturbances	1	12.5	0	0.0	NS	
Total	2	25.0	1	14.2	NS	

\* Fisher exact test

group but the difference between them was not significant (Table 3).

In Quebrada Honda, of 8 cases and 7 controls, 25% and 14.2% respectively had electrocardiographic alterations including a right bundle branch block in the cases group, with an odds ratio of 2.0. However, the difference between cases and controls was not statistically significant (Table 2). In the locality of Poneloya, few seropositives were found as to perform the electrocardiographic assessment.

## DISCUSSION

The serological indicator is a tool for monitoring the index of exposure to *T. cruzi* in populations. This method has been chosen for evaluating transmission of the disease in endemic areas under pesticide treatment, as in Argentina and Brazil <sup>7, 13</sup>. Although control measures for Chagas' disease have not been established in Nicaragua, it is important to be aware of the situation of this disease for the purpose of future monitoring.

The overall prevalence found in this study (7.1%) is close to the lower WHO <sup>17</sup> reported limit, ranging between 6 and 30% according to the zones. A comparison of the results for each one of the communities showed that the Santa Rosa prevalence (13.1%) is similar to that reported in Guatemala (14%) and Costa Rica (11%) <sup>18</sup>. In the other two communities the prevalence rates (4.3 and 3.2%) were relatively low.

The differences in prevalence between the studied communities could be due to different ecological and socioeconomical conditions. Likewise, in Guatemala <sup>11</sup> percentages ranging from 10 to 40% were reported, and in Argentina, CHUIT <sup>6</sup> reports up to 30% in areas where preventive measures have not been taken.

In the analysis of prevalence by age group for the Santa Rosa community an ascending curve was obtained which begins with 5% in the 0 to 5 years old group and reaches 53% in the over 50 age group. This profile corresponds to an endemic zone of long standing, where transmission has been continuous and remains active.

**TABLE 3**  
Condition of the electrocardiogram by age group in cases and controls from Santa Rosa, (Somoto), Nicaragua, 1989.

Age group	EKG cases (n=31)				EKG controls (n=37)				p
	Abnormal No.	%	Normal No.	%	Abnormal No.	%	Normal No.	%	
0 to 24	2	22.2	7	77.8	3	18.8	13	81.3	0.61 *
25 to 44	2	22.2	7	77.8	3	21.4	11	78.6	0.96 <sup>b</sup>
over 45	8	61.5	5	38.5	4	57.1	3	42.9	0.60 *
Total	12	38.7	19	61.3	10	27.0	27	73.0	

a: Fisher exact

b: Chi-square

Higher limits have been reported by CHUIT <sup>6</sup> in an Argentinian endemic zone.

In Quebrada Honda the seropositivity by age group produced an irregular curve, with a first ascending segment up to 19 years, similar to that from Santa Rosa, followed by a plateau up to 39 years and a steep increase from 50 years onwards. The latter was also observed by BONET <sup>1</sup> in an Argentinian endemic zone. For this community, the immunological profile indicates an endemic zone of long standing where transmission is active but at low level.

In the zone of PoneLOYa, an immunological profile could not be obtained because there were only 9 seropositives, but it is noteworthy that 3 of these belonged to the 40 to 49 years group and another 3 were under 9 year old children with parasitemia and Romaña-Mazza sign.

Higher seropositivity rates were observed in dwellers of bad quality houses in the first two communities, but the difference was not statistically significant. In the third locality, the seropositivity was associated with good housing condition. The relative abundance of good type houses in this zone and a high adaptative capability of the vector insect could explain this association.

The relationship between characteristics of the houses and transmission of Chagas' disease has been well studied. In Ojo de Agua, Costa Rica, ZELEDON <sup>19</sup> found correlation between the characteristics of houses and the efectivity of transmission.

In all three zones, females tended to be more frequently infected: 15.3% females vs. 11.3% males in

Santa Rosa; 4.1 vs. 2.8% in Quebrada Honda and 3.3 vs. 0.8% in PoneLOYa. Although the difference was not statistically significant, this occurrence would have a strong influence upon prevalence of the disease, due to the possibility of congenital transmission.

The geometric mean of titres (GMT) has been widely used in seroepidemiological studies of malaria <sup>3</sup> to evaluate the intensity and frequency of reinfections, but there is no reference about the use of this parameter in Chagas' disease surveys. In the present study the GMT for Santa Rosa was 153.6, and for Quebrada Honda, 34.9. In this regard, it could be speculated that the level of titres could have a relationship with pathological changes. This poses a question to be approached in future studies.

One of the main alterations of Chagas' disease is an acute or chronic myocarditis <sup>17</sup>. The rural myocardopathy indexes are also used to assess the increase, decrease, or disappearance of Chagas' disease <sup>10</sup>.

Electrocardiographic abnormalities consisting in left atrioventricular block, sinus bradycardia, decreasing of R wave and anterior wall repolarization disturbances, were found more frequently in the cases group from Santa Rosa. ZICKER et al. <sup>20</sup> have shown that in seropositive asymptomatic individuals the prevalence of EKG abnormalities is higher than in seronegatives. In the present study, the frequency of electrocardiographic changes in the seropositives was not significantly different from the seronegatives. This could be due to an insufficient number of cases studied. Of the Quebrada Honda studied seropositives, one presented right bundle branch block, which is suggestive of chagasic cardiomyopathy. MAGUIRE et al. <sup>10</sup> have stated that a chagasic endemic zone can be recognized



by EKGs presenting: a) 20% of right branch bundle block and b) a marked disproportion of right to left bundle branch block. Likewise, GOLDSMITH et al. <sup>9</sup> reported that the right bundle branch block and ventricular extrasystoles were significantly more frequent in seropositive individuals.

CARRASCO et al. <sup>5</sup> reported that 40% of seropositive individuals without clinical, electrocardiographic or radiological signs of cardiomyopathy, have evidence of apical asynergy, and that many asymptomatics have myocardial deficiencies, as detected by other methods.

It is known <sup>10,15</sup> that it is difficult to establish when an asymptomatic, infected individual can be considered a cardiopath, for it has been demonstrated that there is no relationship between the histopathological changes and clinical manifestations. MAGUIRE et al. <sup>10</sup> reported that electrocardiographic abnormalities occur frequently between 25 and 44 years of age. Similarly, PLESS et al. <sup>12</sup> found a higher frequency of electrocardiographic alterations in less than 35 years old seropositives. In the present study, no relationship between electrocardiographic abnormalities and age group was found. To assess this indicator better, it is necessary to study a greater number of individuals in this age group and to use more sensitive diagnostic methods as ecocardiogram or dynamic electrocardiography and ergometry.

## RESUMO

### Estudio seroepidemiológico y clínico de la enfermedad de Chagas en Nicaragua

Con el objetivo de determinar la prevalencia, perfil inmunológico de la población y conocer las alteraciones electrocardiográficas; se realizó un estudio seroepidemiológico y clínico de la enfermedad de Chagas en tres localidades ubicadas al Norte, Oriente y Occidente de Nicaragua.

Como muestra se tomó suero a 803 personas, a las que se les realizó búsqueda de anticuerpos anti *T. cruzi* por Inmunofluorescencia (IFI) y Hemaglutinación Indirecta (HAI). Al total de los pacientes de dos de éstas localidades que resultaron con serología positiva, se les evaluó por electrocardiografía, estableciendo un grupo control con seronegativos con las mismas características de edad y sexo.

La prevalencia de anticuerpos fué de 13.1, 4.3, y

3.2% en las tres localidades respectivamente. En las dos primeras el perfil inmunológico corresponde al de una zona endémica de vieja data, donde la transmisión ha disminuído y en la tercera a una zona bajo control.

En los seropositivos se encontraron alteraciones electrocardiográficas compatibles con la enfermedad de Chagas pero al comparar con los controles, no se encontró diferencia estadísticamente significativa. Se concluye que la enfermedad es endémica en las tres comunidades y el aspecto clínico requiere un estudio más amplio usando métodos adicionales que permitan evaluar mejor el problema.

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