

Rev. Inst. Med. trop. S. Paulo
46(6):299-302, November-December, 2004

AMERICAN TRYPANOSOMIASIS AND ELECTROCARDIOGRAPHIC ALTERATIONS AMONG INDUSTRIAL WORKERS IN SÃO PAULO, BRAZIL

Moisés GOLDBAUM(1), Fabio Yoshito AJIMURA(1), Júlio LITVOC(1), Silvino Alves de CARVALHO(2) & José ELUF-NETO(1)

SUMMARY

In this article, we evaluate electrocardiographic (ECG) alterations among urban workers from a mechanical-metallurgical industry in São Paulo, Brazil. In a cross-sectional survey carried out in 1980, we found 2.2% positive serological testing for *Trypanosoma cruzi* infection among 27,081 workers. A comparison between seropositive workers and a random sample of seronegative workers frequency-matched by age and occupation revealed that seropositive workers had a much lower educational level, and that a higher proportion of seropositive workers had ECG abnormalities (42.7%) when compared to those negative for *T. cruzi* infection (19.8%). The high frequency of ECG abnormalities suggests the need to provide medical assistance to these workers, without any kind of discrimination and to bring in a form of management that would decrease this dangerous risk to the workers and people around them.

KEYWORDS: Chagas disease; Cardiomyopathy; Cross-sectional study; Industrial workers.

INTRODUCTION

American trypanosomiasis, also known as Chagas disease, is an endemic zoonosis caused by the protozoan parasite *Trypanosoma cruzi*⁶, whose life cycle involves mammalian hosts (including humans) and insect vectors (various species of triatomines⁵). This typical tropical disease is found throughout the American continent, from the south of Argentina to the south of the USA¹¹. The process of urbanization occurring in Latin America has changed the geographic distribution of Chagas disease. This urbanization is also responsible for the development of newer and important ways of transmission.

A survey by the Pan American Health Organization indicates 16 to 18 million people infected with the parasite on the American continent and 90 million exposed to the risk of being infected¹³. In Brazil, it is estimated that about 5 million people were infected in the 1980's⁸. Over recent decades, there has been a large increase in the number of infected people living in urban areas. This increase has been mainly due to migration from rural areas¹⁹, and secondarily to blood transfusion¹⁶.

The most important clinical manifestation of Chagas disease is cardiac. Electrocardiographic (ECG) changes seem to be the most common heart alteration in this disease²¹. The great majority of studies on ECG changes among individuals infected with *T. cruzi* have been conducted in rural endemic areas or clinical settings⁷. The aim of the

present research was to evaluate ECG alterations related to Chagas disease among urban workers in a mechanical-metallurgical industry. We also investigated whether time of residence in a rural area during the first five years of life was associated with ECG alterations.

SUBJECTS AND METHODS

A cross-sectional survey for American trypanosomiasis infection was carried out in 1980 among urban workers from a mechanical-metallurgical industry of the Metropolitan Area of São Paulo, Brazil⁹. We screened 27,081 workers from this industry with a blood sample collected by finger prick onto filter paper; eluates were tested for anti-*Trypanosoma cruzi* antibodies using immunofluorescence. The seropositive and a random sample of seronegative workers in the first test were invited to have a new blood sample collected by venopuncture. The seronegative (approximately 2:1) were frequency-matched to seropositive workers by age and occupation. Only eight women were seropositive; they were excluded. Participants were interviewed using a standardized questionnaire, and an electrocardiogram was performed, with five complex in median per derivation and a long D2 with twenty complex in median.

At a second stage, three serological tests for *T. cruzi* infection were performed on the blood samples: immunofluorescence², hemagglutination³ and complement fixation¹⁸. Individuals found positive in two or three of the tests were considered seropositive for *T.*

(1) Departamento de Medicina Preventiva, Faculdade de Medicina da Universidade de São Paulo, SP, Brasil.

(2) Departamento de Doenças Infecciosas e Parasitárias, Faculdade de Medicina da Universidade de São Paulo, SP, Brasil.

Correspondence to: Moisés Goldbaum, Departamento de Medicina Preventiva, Faculdade de Medicina da Universidade de São Paulo, Av. Dr. Arnaldo 455, 2º andar, 01246-903 São Paulo, SP, Brasil. e-mail: mgoldbau@usp.br

cruzi infection. Those negative in all three serological tests were classified as seronegative.

Electrocardiograms were recorded in 12 standard derivations (long D2) with the subject at rest. They were independently interpreted by two of us (MG, JEN), without knowledge of the serological status. In those cases involving disagreement between the two readers, electrocardiograms were reviewed by both to reach a final classification.

Chi-square for linear trend was used to test statistical significance between seropositive and seronegative workers according to educational level. To estimate the association between seropositive and ECG abnormalities, odds ratios (OR) with 95% confidence intervals (95% CI) were calculated using non-conditional logistic regression¹ (Stata Corp. Stata Statistical Software; Release 6.0. College Station, TX. Stata Corporation).

RESULTS

The first screening of the 27,081 workers found 591 (2.2%) individuals with positive serological test onto filter paper for *T. cruzi* infection. At the second stage, we recovered 373 seropositive workers. The seropositive workers were slightly older (mean = 35.5 years; median = 34.0) than the seronegative workers (mean = 34.2; median = 33.0). The distribution by age-group and educational level is shown in Table 1. Workers infected with *Trypanosoma cruzi* had a much lower educational level than seronegative workers (χ^2 for linear trend = 50.89, $p < 0.001$).

A higher proportion of seropositive workers had ECG abnormalities when compared to those negative for *T. cruzi* infection. Some alteration was found in 156 (42.7%) of the seropositive and in 110 (19.8%) of the seronegative cases (Table 2). A large difference was observed in all age groups, especially among workers less than 40 years old. The OR of any ECG abnormality associated with seropositivity, adjusted for age and educational level, was 3.05 (95% CI 2.23 - 4.17).

Five types of ECG alteration (complete right bundle branch block - CRBB -, left anterior hemiblock - LAH -, ventricular extrasystoles - VE -, 1st degree A-V block - 1st AVB - ventricular repolarization alteration - VRA) were associated with *T. cruzi* infection after adjustment for age and educational level (Table 3). The strongest association was observed with CRBB (OR = 34.40, 95% CI 10.41 - 113.67). No other ECG

Table 1
Distribution of *T. cruzi* seropositive and seronegative workers by age and years of study

Age (years)	Seronegative workers		Seropositive workers	
	N	(%)	N	(%)
15 - 24	75	13.0	25	6.7
25 - 29	114	19.8	75	20.1
30 - 34	138	24.0	89	23.9
35 - 39	91	15.8	73	19.6
40 - 44	70	12.1	52	13.9
45 - 49	54	9.4	36	9.6
50+	34	5.9	23	6.2
Total	576	100.0	373	100.0
Years of study*				
< 4	85	14.8	119	31.9
4	282	49.1	186	49.9
5 - 7	91	15.9	39	10.5
8	56	9.8	13	3.5
> 8	60	10.5	16	4.3
Total	574	100.0	373	100.0

*Data missing for two seronegative workers; $p < 0.001$.

Table 2
Frequency of any ECG alteration* among seropositive and seronegative workers according to age

Age (years)	Seronegative		Seropositive	
	Number	ECG alteration N (%)	Number	ECG alteration N (%)
15 - 24	72	13 18.1	25	14 56.0
25 - 29	107	26 24.3	73	27 37.0
30 - 34	133	17 12.8	88	36 40.9
35 - 39	89	12 13.5	70	29 41.4
40 - 44	69	12 17.4	52	16 30.8
45 - 49	53	20 37.7	34	22 64.7
50+	33	10 30.3	23	12 52.2
Total	556	110 19.8	365	156 42.7

* Data for electrocardiogram missing for 20 seronegative and eight seropositive workers.

Table 3
Prevalence of ECG alteration in industrial workers according to the *Trypanosoma cruzi* serology

ECG	Seronegative		Seropositive		Odds ratio	Odds ratio*	95% CI
	N	(%)	N	(%)			
CRBB	3	0.5	53	14.5	31.31	34.40	(10.41 - 113.67)
LAH	7	1.3	11	3.0	2.44	2.01	(0.74 - 5.41)
VE	10	1.8	33	9.0	5.43	6.04	(2.85 - 12.79)
1 st AVB	3	0.5	16	4.4	8.45	9.11	(2.49 - 33.38)
VRA	10	1.8	19	5.2	3.00	2.73	(1.19 - 6.26)
ANY	110	19.8	156	42.7	3.03	3.03	(2.23 - 4.17)

* Adjusted for age and educational level; CRBB = complete right bundle branch block; LAH = left anterior hemiblock; VE = ventricular extrasystoles; 1st AVB = 1st degree A-V block; VRA = ventricular repolarization alteration; ANY = any alteration.

alteration type was found with a significant difference between seropositive and seronegative individuals. We did not observe inactive myocardial areas.

A possible effect of time spent living in an endemic area for heart damage was investigated in the seropositive group. The presence of any ECG abnormality did not differ according to the number of years spent in a rural region during the first five (Table 4) or ten years of life (data not shown). Nor was any association either was found with regard to the most frequent ECG alterations.

Table 4

Time of residence in rural area within the first five years of life and prevalence of any ECG alterations among seropositives*

Number of years	Total	ECG alterations N (%)
0	47	19 (40.4)
1	1	0 (0.0)
2	8	5 (62.5)
3	7	4 (57.1)
4	8	4 (50.0)
5	287	120 (41.8)

*Data missing for 15 individuals.

DISCUSSION

Cardiopathies are the most important manifestations of Chagas disease and they can be measured by the electrocardiogram. Many studies have shown that there are strong associations between certain specific alterations and this trypanosomiasis^{4,8,12,14}. The findings in this study agree with earlier research in the field demonstrating a statistically significant higher prevalence of any kind of ECG abnormality in seropositive than in seronegative for *T. cruzi* infection. The specific types of ECG alterations related to the infection were VE, CRBB, LAH, 1st AVB and VRA. We found higher prevalence of ECG alterations in all age groups. The high prevalence of ECG alterations in seropositive workers under 40 years of age confirms a relatively short incubation period for development of chronic Chagas cardiomyopathy.

Specifically, CRBB is the most characteristic alteration in the electrocardiogram of individuals with Chagas cardiopathy. In addition, this alteration has a great importance because it represents, among others one of the leading cause of mortality¹⁴.

We detected that urban workers infected with *T. cruzi* have precocious ECG alterations when compared with seronegative workers. These alterations are of particular importance since they are, frequently, the first manifestations of Chagas disease, although they do not lead to clinical symptoms. In this situation, healthy urban workers infected with *T. cruzi* could be unaware of their clinical status, especially the cardiac. Exposure to heavy and dangerous activity at work could worsen the course of the disease¹⁰.

Our study corroborates previous data indicating that seropositives for *T. cruzi* have a higher risk of developing ECG alterations and, consequently, cardiopathy. Regarding the association of the infection with poor social-economic conditions, measured by educational level,

these people are exposed to hard working conditions, especially in urban areas. We have shown that workers infected with *Trypanosoma cruzi* had a much lower educational level than seronegative workers. This confirms previous observations.

A few factors have been postulated for the development of Chagas cardiopathy in infected individuals, including immunological factors, reinfections and physical exertion. MAGUIRE *et al.*¹² investigated the possible effect of physical activity and time of residence in rural areas for the development of Chagas cardiopathy. We tried to correlate time of residence in an rural area (rural area considered as an indirect marker of an endemic area for Chagas disease) and cardiopathy, as measured by electrocardiogram, since more time in such area would lead to higher levels of parasitemia and a greater possibility of developing cardiopathy related to trypanosomiasis. According to these data, presence of positive epidemiological data, such as living in an endemic area in the earliest years of life, could be a reason for treatment, decreasing the viral load and the parasitemia, leading to less alteration in the cardiac muscle²⁰. However, in this survey, in agreement to MAGUIRE *et al.*¹², we determined that the number of years spent in an endemic region during the first five or ten years of life was not associated with cardiac manifestations, as indicated by ECG abnormality.

In conclusion, the high frequency of those manifestations found suggests the necessity of providing medical assistance to these workers^{15,17}, without any kind of discrimination, and of bringing in a form of management that would decrease dangerous risk to the worker and the people around them.

RESUMO

Doença de Chagas e alterações eletrocardiográficas entre trabalhadores industriais em São Paulo, Brasil

Neste artigo, analisamos a frequência de alterações eletrocardiográficas (ECG) em trabalhadores de indústria mecânico-metalúrgica de São Paulo, Brasil. Num estudo transversal, conduzido em 1980, encontramos 2,2% de reações sorológicas positivas para infecção pelo *Trypanosoma cruzi* entre 27.081 trabalhadores. Uma comparação entre trabalhadores soropositivos e uma amostra aleatória de trabalhadores soronegativos pareados por frequência em idade, e ocupação mostrou que os trabalhadores soropositivos apresentam menor nível de escolaridade e maior proporção de alterações ECG (42.7%) quando comparados aos soronegativos para infecção pelo *T. cruzi* (19.8%). A alta frequência de alterações ECG sugere a necessidade de oferecer assistência médica para esses trabalhadores, destituída de qualquer tipo de discriminação, criando condições para diminuir os riscos para esses trabalhadores e os indivíduos próximos.

REFERENCES

- BRESLOW, N.E. & DAY, N.E. - **Statistical methods in cancer research: the analysis of case-control studies**. Lyon, International Agency for Research on Cancer, 1980. v. 1. (Publication No. 32).
- CAMARGO, M.E. - Fluorescent antibody test for the serodiagnosis of American Trypanosomiasis. Technical modification employing preserved culture forms of *Trypanosoma cruzi* in a slide test. *Rev. Inst. Med. trop. S. Paulo*, 8: 227-234, 1966.
- CAMARGO, M.E.; HOSHINO, S. & SIQUEIRA, G.R.V. - Hemagglutination with

- preserved sensitized cells, a practical test for routine serologic diagnosis of American trypanosomiasis. **Rev. Inst. Med. trop. S. Paulo**, 15: 81-85, 1973.
4. CASTRO, C.; PRATA, A. & MACEDO, V. - Estudo clínico durante 13 anos de 190 chagásicos crônicos de Mambá, Goiás, Brasil. **Rev. Soc. bras. Med. trop.**, 34: 309-318, 2001.
 5. CARVALHO, M.E.; SILVA, R.A.; RODRIGUES, V.L.C.C. & OLIVEIRA, C.D. - Programa de controle da doença de Chagas no Estado de São Paulo: sorologia de moradores como parte de investigação de unidades domiciliares com presença de triatomíneos vetores na década de 1990. **Cadern. Saúde públ. (Rio de J.)**, 18: 1695-1703, 2002.
 6. CHAGAS, C. - Nova tripanozomiaze humana: estudos sobre a morfologia e o ciclo evolutivo do *Schizotrypanum cruzi* n. gen., n. sp., agente etiológico de nova entidade mórbida do homem. **Mem. Inst. Oswaldo Cruz**, 1: 159-218, 1909.
 7. COURA, J.R.; BORGES-PEREIRA, J.; ALVES FILHO, F.I. *et al.* - Morbidity of Chagas' disease in areas of Sertão da Paraíba and Caatinga do Piauí. **Rev. Soc. bras. Med. trop.**, 29: 197-205, 1996.
 8. FERREIRA, M.S.; LOPES, E.R.; CHAPADEIRO, E.; DIAS, J.C.P. & OSTERMAYER, A.L. - Doença de Chagas. In: VERONESI, R. **Tratado de Infectologia**. São Paulo, Atheneu, 1996. p. 1175-1213.
 9. GOLDBAUM, M. - **Saúde e trabalho: a doença de Chagas no setor industrial**. São Paulo, 1981. (Tese de doutorado - Faculdade de Medicina da Universidade de São Paulo).
 10. GUARIENTO, M.E.; CAMILO, M.V.F. & CAMARGO, A.M.A. - Working conditions of Chagas' disease patients in a large Brazilian city. **Cadern. Saúde públ. (Rio de J.)**, 15: 381-386, 1999.
 11. KIRCHOFF, L.V. - American trypanosomiasis (Chagas' disease): a tropical disease now in the United States. **New Eng. J. Med.**, 329: 639-644, 1993.
 12. MAGUIRE, J.H.; HOFF, R.; SHERLOCK, I. *et al.* - Cardiac morbidity and mortality due to Chagas' disease: prospective electrocardiographic study of a Brazilian community. **Circulation**, 75: 1140-1145, 1987.
 13. PAN AMERICAN HEALTH ORGANIZATION - **Health conditions in the Americas**. Washington, PAHO, 1994. p. 147-149. (Scientific Publication No. 549)
 14. PRATA, S.P.; CUNHA, D.F.; CUNHA, S.S.F.; PRATA, S.C. & NOGUEIRA, N. - Prevalência de alterações eletrocardiográficas em 2000 pacientes chagásicos idosos e não idosos. **Arq. bras. Cardiol.**, 60: 369-372, 1993.
 15. RAMOS Jr., N.A. & CARVALHO, D.M. - Os diferentes significados da certificação conferida ao Brasil como estando livre da doença de Chagas. **Cadern. Saúde públ. (Rio de J.)**, 17: 1403-1412, 2001.
 16. SALLES, N.A.; SABINO, E.C.; CLIQUET, M.G. *et al.* - Risk of exposure to Chagas' disease among seroreactive Brazilian blood donors. **Transfusion**, 36: 969-973, 1996.
 17. UCHOA, E.; FIRMO, J.O.A.; DIAS, E.C.; PEREIRA, M.S.N. & GONTIJO, E.D. - Signos e significados e ações associadas à doença de Chagas. **Cadern. Saúde públ. (Rio de J.)**, 18: 71-79, 2002.
 18. WADSWORTH, A.B.; MALTANER, F. & MALTANER, E. - The quantitative determination of the fixation of complement by immune serum and antigen. **J. Immunol.**, 21: 313-340, 1931.
 19. WANDERLEY, D.M. & CORREA, F.M. - Epidemiology of Chagas' heart disease. **Rev. paul. Med.**, 113: 742-749, 1995.
 20. ZHANG, L. & TARLETON, R.L. - Parasite persistence correlates with disease severity and localization in chronic Chagas' disease. **J. infect. Dis.**, 180: 480-486, 1999.
 21. ZICKER, F.; NETTO, J.C.A.N.; ZICKER, S.E.M.; OLIVEIRA, R.M. & SMITH, P.G. - *Trypanosoma cruzi* infection and electrocardiographic findings among active manual workers. A population-based study in Central Brazil. **Int. J. Epidem.**, 19: 182-186, 1990.

Received: 26 April 2004

Accepted: 6 October 2004