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Treatment Patterns and their Relation to the Diagnosis of Chagas Disease in Patients with Heart Failure, 2001-2011: Bogotá, Colombia

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ABSTRACT

Chagas (CH) disease, found throughout Latin America, is caused by the parasite *Trypanosoma cruzi*. Heart failure is a common (i.e. 10-30%) late outcome for people who develop symptomatic Chagas disease. Studies show that patients with Chagasic heart failure have a worse prognosis than patients with heart failure from other aetiologies. As most people living with CH are from lower socioeconomic backgrounds where access to quality medical care can be limited, the study investigated the equality of patient care between Chagas and non-Chagas heart failure patients in La Fundación Cardioinfantil (FCI), Bogotá, Colombia.

Methods **The study was a retrospective cohort study, compiling data from medical files of patients hospitalized for heart failure between 2001-2011. Each CH patient (n=41) was matched with 1-2 comparable non-Chagas (no-CH) patients (n=77).**

Results/Projected Outcomes **At the FCI, no differences were observed between care given to CH and no-CH patients, concluding that patients with CH receive a similar standard of care to patients with no-CH. Because this report is not inclusive of other health institutions in Colombia, the FCI is recommended as a model institution for equal patient treatment.**

Keywords: Chagas disease, heart failure, treatment equality, Colombia, *Trypanosoma cruzi*

INTRODUCTION

Chagas disease is common throughout Latin America and is caused by the protozoan parasite *Trypanosoma cruzi*, most commonly transmitted by a blood-sucking triatomine bug.[23, 15] Chagas disease is epidemic in Latin America. It is a disease with important social and economic implications as the majority of infected and at-risk populations are from lower socioeconomic and rural settings.[21, 4, 25, 19] Heart failure is a common (i.e. 10-30%) late outcome for people who develop symptomatic Chagas disease, and studies show that patients with Chagasic heart failure have a worse prognosis than patients with heart failure from other aetiologies.[24, 9, 17, 21, 28, 13, 10] In the absence of specific evidence indicating otherwise, treatment for heart failure in Chagasic patients follows similar protocols as treating patients without Chagas disease. As most people living with Chagas disease are from lower socioeconomic backgrounds, access to medical care is limited and patients with Chagas disease may receive poorer quality care when compared to non-Chagas patients.[4]

To test this hypothesis, the intention behind the study was an inter hospital comparison between medical institutions in Colombia on the quality of care received by heart failure patients whose aetiology was or was not Chagas disease. However, due to time and resource restraints, we were only able to obtain data from Fundación Cardioinfantil (FCI) – a private non-profit hospital with level IV complexity located in the North of Bogotá in a developed and middle-class neighbourhood. Further research on treatment equality is recommended in different medical institutions in Colombia.

BACKGROUND

Between 8-10 million people are infected with Trypanosoma cruzi and over 100 million people are at risk in Latin America.[21, 28, 13] Studies over the past decade in Colombia estimate between 0.7 and 1.3 million people are infected with T. cruzi, and between 3-8 million more Colombians are at-risk of infection.[6, 4, 18] The majority of people exposed to Chagas disease live in poor rural areas of Colombia with inadequate housing.[4] However, influenced by Colombia's on-going internal conflict and changing economics, urbanization has increased from 31% in 1938 to around 75% in 2010[12, 7], bringing populations from high-risk Chagas areas to cities and surrounding slums.[14] Studies estimate that over 95% of people displaced from rural areas are never tested for T. cruzi infection, largely due to limited diagnostic services and low numbers of people donating blood.[4] (all blood donors in Colombia are tested for T. cruzi). Given that infection by T. cruzi is greatest among Colombia's most vulnerable populations, there is a significant gap between the number of actualized diagnostic tests and the number of people untested and thus untreated.[10]

There are two main phases of Chagas disease: acute and chronic. The acute phase occurs after initial exposure, lasting four to six weeks.[13] This phase is generally asymptomatic although it can result in mild symptoms, including fever and swelling around the site of initial infection. The main treatment option for the acute phase of Chagas disease is Benznidazole[5] available in Colombia since 2000.[20] Benznidazole is most effective if taken during the acute stage (60-80% cure rates), but has low effectiveness in patients who develop chronic Chagas disease (10-20% cure rates) and is therefore recommended in Colombia for people with acute and congenital infection and in young children.[4, 25, 28, 13, 10,5] Access to Benznidazole is very limited in Colombia and recent studies report massive global shortages of Benznidazole, thereby hindering Chagas programs and studies.[4, 5, 20]

If left untreated during the acute stage, as most cases are, people enter a lifelong chronic stage of the disease that is either asymptomatic or symptomatic. The majority of people with known Chagas disease are asymptomatic (60-70%), remaining in an indeterminate stage.[28] However, 10-30% of infected people in Colombia will develop Chronic Chagas Heart Disease (CCHD), a chronic cardiomyopathy that can progress to heart failure.[21, 28, 13, 10] When infected patients develop CCHD, their prognosis appears worse than in other similar dilated cardiomyopathies.[9, 17, 2] At least 2/3 of deaths in patients with CCHD are attributed to sudden cardiac death.[10]

METHODS

We attempted to address the hypothesis that patients with Chagas disease receive a poorer quality of medical attention when compared to people treated for the same illness without Chagas disease. Patients who fit the inclusion criteria were admitted to the FCI between 2001-2011 for heart failure. The study retrospectively compared a cohort of 41 CH and 77 comparable (see "matching" below) no-CH patients, reviewing patient files and recording their health management while hospitalized.

Inclusion Criteria

The inclusion criteria for patients hospitalized for 'heart failure' had to comply with a minimum two of the following three qualifications:

- Diagnosis of heart failure upon hospital admission, as defined by *Guías colombianas sobre la evaluación y el manejo de la falla cardíaca crónica del adulto* (Colombian guide about the evaluation and management of chronic heart failure in adults)[11];
- Administration of intravenous diuretics during hospitalization; and

- Pulmonary Oedema, as defined by A.D.A.M. Medical encyclopaedia, identified in patient chest x-ray results.[29]

Exclusion Criteria

The study excluded patients whose heart failure diagnosis was secondary to a valvular heart disease diagnosis.

Matching

Each Chagas patient was matched with two non-Chagas controls to increase statistical power, using the following criteria:

- No more than 5% difference of the 'left ventricular ejection fraction,' found on the patient's echocardiogram.[22] Matching by ejection fraction was a measure used to compare patients in similar stages of heart failure. Ejection fractions of 50% and above were matched with an ejection fraction at a minimum of 45% and with no maximum cap. Patients with no ejection fraction reported were considered as 50% and above, because disqualifying participants from the study for not having an echocardiogram would have been counterproductive to the study's measurable objectives.

- No more than five years difference in age;

- No more than six months difference in date of hospital admittance (to eliminate bias due to advances in diagnosis or treatment of heart failure during the study period).

Classifications

After hospital admissions, patients were classified according to the New York Heart Association functional classification (NYHA), and were subjected to echocardiograms to determine ejection fraction. Classes II and I were analysed together and classes III and IV were analysed together. [1, 16, 26]

Echocardiogram

Studies on Chagas disease suggest using echocardiograms as a valuable, non-invasive tool to assess heart function and the risk of mortality and morbidity in patients with CCHD, at a reduced cost compared to other cardiac evaluation methods.[1, 2, 22, 24, 27] In addition, studies report using the left ventricular ejection fraction as a good indicator of patient morbidity and a predictor of mortality.[1, 3, 17, 22, 27]

Data Extraction and Analysis

A list of patients diagnosed with Chagas disease between 2001 and 2011 was obtained in the FCI's department of patient archives. To match CH cases with no-CH controls, a list of patients hospitalized for heart failure between 2001 and 2011 was also obtained in the department of patient archives. Cases and controls were screened for inclusion criteria, and a maximum of two controls were matched to each case based on matching criteria. Information regarding patient demographics, parasitology, clinical diagnostics and management of health during hospitalizations, including pharmacology, was collected directly into a data extraction form on Microsoft Access 2003, and stored in an encrypted and password protected Access database.

Data was transferred into SPSS 2005 for quantitative analysis of frequencies, Chi-squared (X^2) tests, Kruskal-Wallis analysis of variance and Kaplan-Meier survival function. Backups were stored on two computers used by researchers and both computers were password protected. An internal institutional review approved the study protocol and ethics. No personal information was collected from files that would be traceable to patients.

RESULTS

Patient Demographics

Of 148 eligible Chagas patients, 41 met inclusion criteria. The 41 CH cases were matched with 77 no-CH controls. Three CH cases were matched with only one no-CH control, and one CH case was unable to be matched with any controls. Of the 41 CH patients, 29.3% discovered their Chagas disease diagnosis during hospitalization. Causes of hospitalization were similar in CH and non-CH patients, with 85.4% and 90.9% of patients hospitalized for heart failure. Additional causes of hospitalization were de Novo Heart Failure, arrhythmias, and ischemia, which was significantly different between CH and no-CH **(Table 1)**.

All patients in the study were diagnosed with heart failure and received IV diuretics, and apparently fewer patients with CH (26.8%) were diagnosed with pulmonary oedema than no-CH patients (45.4%, p-value 0.048). Results showed no significant differences in patient demographics and clinical assessment including age, sex, NYHA, mean days hospitalized, and hospitalizations for heart failure one year prior to hospitalization **(Table 1)**. There was no significant difference in mortality between CH (12.2%) and no-CH (3.9%) patients (X^2 = 2.916, p-value = 0.088).

Pharmaceutical Results

The pharmaceutical management upon admission was similar for ACE inhibitors (65.9% in CH versus 50.9% in no-CH), beta-blockers (61% versus 64.4%), and Spironolactone (65.9% versus 58.4%), but slightly different for angiotensin II receptors antagonists (4.9% versus 18.2%, p=0.044) **(Figure 1)**.

Clinical and Procedural Care

During hospitalization, there were no differences with respect to implantable cardioverter-defibrillators or pacemakers. However, during previous hospitalizations at FCI, more CH patients received an Implantable Cardioverter Defibrillator (ICD)/pacemaker than no-CH patients (36.6%, 16.9% respectively; X^2 = 5.738, p-value 0.017). CH patients received neither revascularization nor heart transplant during all reported hospitalizations. Revascularization during previous hospitalizations was greater for no-CH patients (18.2%, X^2 = 8.458, p-value 0.004) (**Table 2**). While the re-hospitalization rate is not significantly different, the time until re-hospitalization is significant. Re-hospitalization occurred in 31.7% of CH and 27.3% for no-CH patients, with a median time between hospitalizations of 11 and 5 months, respectively (p-value =0.01).

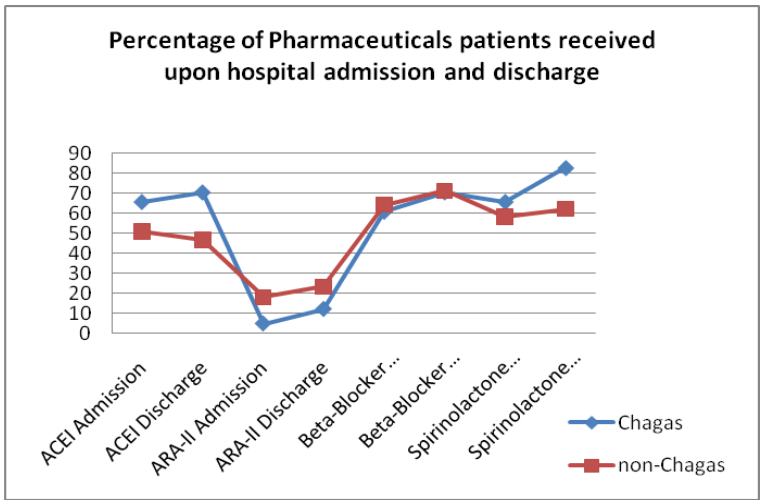

Figure 1 Graphical representation of the percentage of the different pharmaceuticals which patients received at hospital admission and discharge between Chagas and non-Chagas patients

Table 1 Aetiology, demographics and clinical assessment of Chagasic and non-Chagasic patients

ETIOLOGY	CH n (%)	non-CH n (%)	p-value
Contributing Factors of Heart Failure			
Chronic Chagas Cardiomyopathy	41 (100)	0	0
Hypertension	10 (24.4)	56 (72.7)	0
Coronary Heart Disease	1 (2.4)	37 (48.1)	0
Not Reported	0	15 (19.5)	0.002
Causes of Hospitalization			
Decompensated Heart Failure	35 (85.4)	70 (90.9)	0.36
de Novo Heart Failure	2 (4.9)	0	0.051
Arrhythmias and Conduction Blockages	4 (9.8)	3 (2.6)	0.092
Coronary Ischemia	0	18 (23.4)	0.001
Demographics and Clinical Features	**CH n (%)**	**non-CH n (%)**	p-value
Female	14 (34.1)	25 (32.5)	0.854
Age (Mean)[i]	60.61	62.42	0.552
NYHA (I-II)	3 (7.3)	7 (9.1)	0.742
NYHA (III-IV)	30 (73.2)	61 (79.27)	0.456
Mean Days Hospitalized	10	14.7	0.689
Hospitalized for Heart failure 1 Year Prior (Mean)	0.61	0.69	0.266
Mortality	5 (12.2)	3 (3.9)	0.088
Inclusion Criteria	**CH n (%)**	**non-CH n (%)**	p-value
Heart Failure Diagnosis	41	77	
IV diuretic	41	77	
Pulmonary Oedema	11 (26.8)	35 (45.4)	0.048

[i] *Patients were matched by age, date of hospitalization and ejection fraction*

Table 2 Diagnostic tests and procedures performed on patients before, during or after hospitalization, as indicated

DIAGNOSTIC TESTS	CH n (%)	non-CH n (%)	p-value
Chest x-ray	32 (78)	60 (77.9)	0.987
Electrocardiogram	38 (92.7)	74 (96.1)	0.421
Echocardiogram	31 (75.6)	65 (84.4)	0.242
Ejection Fraction (mean)	23.41	27.71	0.18
Holter Monitor Test	9 (22)	11 (14.3)	0.291
Electrophysiology Study	2 (4.9)	0 (0)	0.051
Coronary angiography	3 (7.3)	16 (20.8)	0.058
Cardiac Ventriculography	3 (7.3)	9 (11.7)	0.454
Cardiac Stress Test	3 (7.3)	8 (10.4)	0.585
Cardiac Enzymes	6 (14.6)	9 (11.7)	0.647
PROCEDURES	**CH n (%)**	**non-CH n (%)**	**p-value**
Previous ICD/Pacemaker	15 (36.6)	13 (16.9)	0.017
Recent ICD/Pacemaker	7 (17.1)	9 (11.7)	0.416
Previous Revascularization before	0	14 (18.2)	0.004
Recent Heart Transplant during	0	2 (2.6)	0.298
Valve Replacement	0	1 (1.3)	0.464

DISCUSSION

Results from our study indicate no significant differences in the general clinical and pharmaceutical management of Chagas and non-Chagas patients hospitalized for heart failure at Fundación Cardioinfantil. Significant differences were observed in the contributing factors of heart disease as well as in 'time to re-hospitalization'. All CH patients had chronic Chagas cardiomyopathy that contributed to heart failure. Additional contributing factors to heart failure in CH patients were hypertension (24.4%) and coronary disease (2.4%)[9]. For no-CH patients, 72.7% of heart failure was related to hypertension, 48.1% to coronary disease, and 19.5% not reported. All Chagas patients in the study had chronic Chagas heart disease as their aetiology for heart failure, while contributing factors for heart failure in no-CH patients are hypertension, coronary disease. Unfortunately we did not collect data on other potential risk factors for heart disease (i.e. nutritional status) or coronary heart disease (smoking, hyperlipidaemia, and diabetes).

In patients with CCHD, the heart disease involves direct damage to the conduction fibres over time, and can take decades to develop. Chagasic cardiomyopathy is asymptomatic until later in the disease, developing symptomatically in Chagas patients when the damage to the heart is greater than the heart's mechanisms to compensate for heart failure. Several studies indicate that CCHD is associated with higher mortality and worse prognosis than other aetiologies for heart disease.[25, 24, 9, 17, 2] The worse outcomes associated with CCHD are due to several of the following factors: impaired left ventricular function; NYHA class III-IV; more myocardial destruction than other aetiologies including hypertension and ischemia; more severe ventricular arrhythmias; and social factors influencing treatment and medical care.[24, 9] Although other studies on Chagas disease suggest that CH patients have a worse course of disease than no-CH patients.[25, 24, 9, 17, 2], we observed only a marked but not significant difference in mortality between Chagas patients (12.2%) and non-Chagas patients (3.9%) (P-value = 0.088). Therefore, the general equity observed between CH and no-CH patients at FCI does not support the hypothesis of **inadequate** care for CH patients.

Pulmonary oedema was significantly higher in no-CH patients (45.4%) than CH (26.8%, p-value

0.048). The lower incidence of pulmonary oedema in CH patients may be due to the chronicity of CCHD: Acute cases of heart failure present with more pulmonary oedema than chronic heart failure(Dickstein et al. 2008).
Chagas patients were re-hospitalized at FCI a median of 11 months after the analysed hospitalization, compared with a median of 5 months for no-CH patients. The difference observed in time to re-hospitalization may represent a better control and compliance of heart failure in patients with chronic cardiomyopathy, compared to non-Chagas patients. Our data indicate that a high percentage of CH patients received pacemakers or ICD prior to hospitalization. This supports our findings that Chagas patients at the FCI are treated with equal use of resources as no-CH.

Our hypothesis that patients with Chagas disease receive inferior clinical care is based on the notion that the majority of people living with Chagas disease in Colombia are from poor rural areas[4, 24, 20], and most remain undiagnosed or receive insufficient long-term follow-up.[24, 4] The hospital in which the study was performed, Fundación Cardioinfantil, is a leading private research and cardiology hospital in a middle-class neighbourhood in Northern Bogotá. Chagasic patients from the Southern and poorer areas in and around Bogotá would be more likely to access a hospital closer to their homes due to transportation costs, which may create a bias in the patient populations hospitalized at FCI. An additional bias is the inability to pay for medical services by poorer patients unable to afford health insurance. While Colombia has a form of universal health care, subsidized patients are more likely referred to public hospitals.[20]

The intention of the study was to compare health management of Chagas and non-Chagas patients in a variety of medical institutions in Colombia, however due to time and resource restraints the study was limited to FCI. Similar research implemented in hospitals and clinics located in rural areas or in poorer and less developed areas in Colombia would provide a more well rounded understanding of the treatment patterns of Chagas patients, and may provide further insight into the high mortality in patients with CCHD associated with social and economic disparities (comparing intra and inter hospital treatment and outcome differences).

CONCLUSION

At the FCI, no differences were observed between care given to Chagas and non-Chagas patients hospitalized for heart failure. Therefore, we conclude that at FCI there is no substance to the argument that patients with CH receive a lower standard of care than patients with no-CH. However, it is important to establish that this is not inclusive of other health institutions in Colombia, and we recommend further investigations throughout the country, to include both the public and private sectors. We recommend the FCI be used by other institutions in Colombia as a model institution for equal treatment of Chagas and non-Chagas patients.

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