Hospital Admissions for Tuberculous Pericarditis in the United States 2002–2014

Neiberg de Alcantara Lima1, Christopher Stancic2, Duncan Vos3, Mireya Mireya del Carmen Diaz Insua3, Carol Cavalcante de Vasconcelos Lima4, Ricardo Lessa de Castro Jr1, Rheanne Maravelas5, Thomas A. Melgar5

Departments of 1Internal Medicine, 2Department of Internal Medicine, 3Statistics and 4Pediatrics, Adolescent and Internal Medicine, Western Michigan University Homer Stryker MD School of Medicine, Kalamazoo, Michigan, USA, 5Mario de Assis Radiology Clinic, Fortaleza, Brazil

Abstract

Background: Extra pulmonary manifestations of tuberculosis (TB) are rare in developed countries. TB is the main etiology of chronic pericarditis in developing countries, but it’s epidemiology is not unknown in the United States. Methods: This retrospective study used the Healthcare Utilization Projects/Nationwide Inpatient Sample (HCUPS/NIS) database from 2002-2014 to evaluate the characteristics, risk factors, trends over time and region of tuberculous pericarditis in the United States. Results: The data during the study period consists of 100,790,900 discharges accounting for 482,872,274 weighted discharges. The data showed 744 weighted discharges with indication of both tuberculosis and pericarditis. A co-occurrence of TB pericarditis and malignancy or chronic kidney disease was more common than in patients without TB pericarditis. The frequency of co-occurrence of TB pericarditis and HIV infection, obesity, alcohol abuse and organ transplant was not elevated. Conclusion: TB pericarditis is rare disease in the USA and the classical risk factors for lung tuberculosis may not be associated with TB pericarditis. CKD and malignancy appear to be associated with TB pericarditis, further studies are required to determine causality.

Keywords: Epidemiology, pericarditis, tuberculosis, United States

Submission: 08-10-2019 Accepted: 15-10-2019

INTRODUCTION

Tuberculosis (TB) is a major cause of mortality due to infectious diseases, especially in developing countries. Although it is primarily a disease of the lungs, it has a number of extrapulmonary manifestations that contribute greatly to its mortality and morbidity. One such manifestation is tuberculous pericarditis, which occurs in only 1%–2% of patients with pulmonary TB in endemic areas but has a mortality rate from 17% to 40%.

Tuberculous pericarditis is a far less common complication in developed countries such as the US, with the population at greatest risk being those who immigrated from TB-endemic areas. However, health-care providers in these regions may miss tuberculous pericarditis in their differential due to its low incidence and atypical presentation relative to other types of acute pericarditis.

This study was designed to characterize the current incidence and profile of tuberculous pericarditis in the US, as well as investigate potential risk factors for the disease. This information could help physicians diagnose tuberculous pericarditis earlier, anticipate complications, and reduce mortality from the disease.

Objective

This retrospective study used the Healthcare Utilization Projects/Nationwide Inpatient Sample (HCUPS/NIS) database from 2002 to 2014 to evaluate the characteristics, risk factors, trends over time, and region of tuberculous pericarditis in the United States.

METHODS

This is a retrospective study using the National Inpatient Sample (NIS) to assess the frequency and trend of TB pericarditis in the United States from 2002 to 2014.
The NIS is a database provided by the Health care Utilization Project (HCUP) which is sponsored by the Agency for Healthcare Research and Quality. The National Inpatient Sample contains discharges from the State Inpatient Databases and is designed to represent hospitals and discharges at a national level using a random sampling of discharges stratified by the US census region, urban or rural location, teaching status, ownership, and bed size. The data collected include demographic information and diagnostic and procedural codes that were coded during the patient’s hospital stay. Strengths of the database include the size, with information about millions of patients each year. Limitations include the inability to assess causation or relation between different diagnoses and dependence on the coding during the stay. Only diagnoses that were coded during the hospitalization are reflected in the data.

Descriptive analysis was used to assess the frequency of TB pericarditis and patient characteristics. The proportion (95% confidence interval [CI]) of TB pericarditis, as indicated by inclusion criteria diagnosis codes, is reported for the study period 2002–2014. Inclusion criteria consisted of the presence of at least one indication for TB and at least one indication for pericarditis.

Categorical patient characteristics are reported as frequency (percent), and continuous patient characteristics are reported as median (interquartile range). The distribution of each patient demographic is reported for those with TB pericarditis. To assess the frequency of co-occurrence with TB pericarditis, diagnosis codes were used to create composite variables for HIV, type 2 diabetes mellitus, cancer, transplant recipient, chronic kidney disease (CKD), and alcohol abuse.

Demographic information from the group with TB pericarditis could be compared to patients in the database without TB pericarditis.

Weighted frequencies are reported, and all the analyses are completed using weighted estimates in accordance with the NIS sampling methodology. SAS Studio was utilized for the analysis.

## Results

The data during the study period consist of 100,790,900 discharges accounting for 482,872,274 weighted discharges. The data contain 112,106 TB discharges representing a weighted total discharge count of 539,071 TB cases. The data also contain 73,221 pericarditis discharges representing a weighted total discharge count of 352,671 pericarditis cases. There are 153 discharges that have an indication for both TB and pericarditis, which represent a total of 744 weighted discharges with both TB and pericarditis [Figure 1].

Patient’s median age, length of stay, mortality, payer, costs, and ethnicity are summarized in Table 1.

Of those with TB Pericarditis, 29.1% (95% CI: 24.2, 33.9) have an income in the lowest quartile of incomes within their respective zip code, 28.3% (95% CI: 23.2, 33.5) have an income in the second quartile of incomes within their respective zip code, 24.5% (95% CI: 20.3, 28.7) have an income in the third quartile of incomes within their respective zip code, and 18.0% (95% CI: 12.6, 23.4) have an income in the highest quartile of incomes within their respective zip code.

We found that patients in the low-income quartiles and African-Americans were slightly overrepresented among patients with TB pericarditis compared to the general population. The median age of 61 was older than the median of all patients in the data set (52), but the CI did not suggest a statistically significant difference. Additional information about cost and mortality is available [Table 1].

The following four procedures were identified in the data set: pericardial window, pericardiocentesis, pericardiectomy, and pericardial biopsy. The data contained 69 discharges which account for 338 weighted discharges with TB pericarditis that underwent one of the four procedures. That is, of those with TB pericarditis, 45.46% (95% CI: 37.24, 53.68) underwent one of those four procedures.

### Table 1: General characteristics

| Demographic features      | Number (confidence interval) |
|---------------------------|------------------------------|
| **AGE**                   | 61.0 (49.8, 71.1) years      |
| **length OF STAY**        | 5.7 (2.8, 10.5) days         |
| **IN HOSPITAL MORTALITY** | 6.62% (95% CI 2.66, 10.58)   |
| **COST**                  | US$ 44,811 (18,536-92,014)   |
| **ETHNICITY**             |                              |
| CAUCASIAN                 | 45.6% (95% CI 36.6, 54.7)    |
| AFRICAN AMERICAN          | 19.7% (95% CI 12.6, 26.8)    |
| HISPANIC                  | 15.6% (95% CI 8.9, 22.5)     |
| ASIAN/PACIFIC             | 7.7% (95% CI 3.0, 12.3)      |
| OTHER                     | 11.2% (95% CI 6.0, 16.4)     |
| **Median income per zipcode** |                           |
| First quartile (lowest)   | 29.1% (95% CI 24.2, 33.9)    |
| Second quartile (2nd lowest) | 28.3% (95% CI 23.2, 33.5)    |
| Third quartile (2nd higher)| 24.5% (95% CI 20.3, 28.7)    |
| Forth quartile (higher)   | 18.0% (95% CI 12.6, 23.4)    |
| **Payer**                 |                              |
| Medicare                  | 335 (45.3%)                  |
| Medicaid                  | 196 (26.5%)                  |
| Private insurance         | 120 (16.2%)                  |
| Self payer/other          | 89 (12%)                     |

### Table 2: Co-occurrences

|                      | Patients with TB pericarditis | Patients without TB pericarditis |
|----------------------|------------------------------|---------------------------------|
| HIV                  | Low frequency                | -                               |
| Organ transplant     | Low frequency                | -                               |
| Alcohol abuse        | Low frequency                | -                               |
| BMI                  | 90% marked as unknown        | -                               |
| Type 2 diabetes mellitus | 16.22% (95% CI 10.44, 21.99) | 17.25% (95% CI 17.14, 17.36)    |
| Malignancy           | 21.08% (95% CI 14.48, 27.68) | 7.56% (95% CI 7.44, 7.67)       |
| Chronic kidney disease | 11.97% (95% CI 6.85, 17.08)  | 8.08% (95% CI 8.01, 8.16)       |
Co-occurrences
Of those with TB pericarditis, the frequency of the following co-occurrences was ≤10 and therefore cannot be reported: HIV, organ transplant, and alcohol abuse. Body mass index (BMI) data are also sparse, with 139 of the 153 TB pericarditis having an “unknown” BMI, and therefore cannot be reported.

There are 25 discharges (121 weighted discharges) or 16.22% (95% CI: 10.44, 21.99) of the discharges with TB pericarditis that also had a diagnostic code for type 2 diabetes mellitus, compared to 17.25% (95% CI: 17.14, 17.36) of discharges without TB pericarditis. There are 32 discharges (157 weighted discharges) or 21.08% (95% CI: 14.48, 27.68) of the discharges with TB pericarditis that also had a diagnostic code for cancer, compared to 7.56% (95% CI: 7.44, 7.67) of discharges without TB pericarditis. There are 18 discharges (89 weighted discharges) or 11.97% (95% CI: 6.85, 17.08) of the discharges with TB pericarditis that also had a diagnostic code for CKD, compared to 8.08% (95% CI: 8.01, 8.16) of discharges without TB pericarditis [Table 2].

Table 3 shows the rate of occurrence of TB pericarditis by the US region, as described in Figure 2. Figure 3 shows the proportion (95% CI) of discharges with TB pericarditis for over time. Years were aggregated to avoid the yearly frequency of 10 or less.

Discussion
NIS-HCUP is a large database with more than 480 million admissions over 12 years. Since TB pericarditis has a low prevalence in the USA, only 744 weighted cases were found. Less than 1% of the patients with a diagnosis of TB had an associated pericarditis diagnosis and <1% of the patients of pericarditis had an associated TB diagnosis. While only 1% of TB patients have pericarditis in the US and developing countries, in developing countries with a high prevalence of TB, 70% of cases of large pericardial effusion are attributable to TB, and it is an important etiology of constrictive pericarditis.[2,5,6]

Studies with hospital costs of TB pericarditis are scarce; the mean hospital stay in our study was $44,811 US dollars, four times more than the national average for hospitalizations for other diagnoses over a similar length of stay.[7] Considering the hospitalization length mean was 5.7 days, and the cost only reflects the hospital stay, we can assume that total cost is much higher since medical treatment lasts at least 6 months and often includes additional procedures and rehabilitation.

Known risk factors for TB are immunosuppression or high exposure to infected people. In nonendemic countries, HIV infection, glucocorticoids, diabetes, tumor necrosis factor inhibitors, organ transplant, substance abuse, underweight, malignancy, and chronic renal disease are potential risk factors.[8-14] To our knowledge, prior to our study, there is no specific study of risk factors for TB pericarditis. In our analysis, the number of cases with TB and pericarditis who also had HIV, organ transplant, or alcohol abuse was ≤10. To preserve patient’s privacy, the database does not allow access to results <10; hence, these data are not reportable.
BMI was also poorly reported in our sample. On the NIS database, there is no access to personal information, so we rely on ICD-9 recorded by the physician during the hospitalization, and we believe that BMI is generally underreported. A study of diabetic patients in Taiwan showed diabetes doubles the chance of developing TB.\cite{12} In our sample, the co-occurrence of TB pericarditis and diabetes (16.22%, 95% CI: 10.44, 21.99) was similar to patients without disease and diabetes (17.25%, 95% CI: 17.14, 17.36).

Another study performed in cancer patients at Memorial Sloan-Kettering Cancer Center in New York showed an increased risk of TB in patients with hematological malignancies. We had comparable results in our TB pericarditis group with a co-occurrence of 21.08% in patients with cancer and 7.56% in patients without cancer.\cite{11}

CKD has been shown to be an important risk factor for TB. A possible explanation should be a decrease in cellular immunity caused by uremia and dialysis treatment. In our study, the co-occurrence of TB pericarditis and CKD was reported in 11.97% (95% CI: 6.85, 17.08), whereas 8.08% of the patients without TB pericarditis had CKD.\cite{13,14}

Other factors such as immigration and climate possibly play a role in the prevalence of the disease. We had a higher occurrence of TB pericarditis in Northeast and West. The states are grouped by NIS, as shown in Figure 2, but as the states do not have demographic homogeneity, it is not possible to conclude any particular reason for the difference in the prevalence.

Limitations
As the disease has a low incidence in the USA and this is a cross-sectional study, causality cannot be defined.

During the study period, the database used ICD-9, and there was not a specific code for TB pericarditis. We assumed that patients who had active TB and concomitant active pericarditis had TB pericarditis.

Conclusions
This study provides additional information about the demographics of patients with TB pericarditis in the USA. It is a rare disease in the USA, and the classical risk factors for lung TB may not be associated with TB pericarditis. CKD and malignancy appear to be associated with TB pericarditis; further studies are required to determine causality.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

References
1. Chang SA. Tuberculous and infectious pericarditis. Cardiol Clin 2017;35:615‑22.
2. Syed FF, Mayosi BM. A modern approach to tuberculous pericarditis. Prog Cardiovasc Dis 2007;50:218‑36.
3. Narasimhan P, Wood J, Macintyre CR, Mathai D. Risk factors for tuberculosis. Pulm Med 2013;2013:828939.
4. Mutyaba AK, Ntsekhe M. Tuberculosis and the heart. Cardiol Clin 2017;35:135‑44.
5. Ramasamy V, Mayosi BM, Sturrock ED, Ntsekhe M. Established and novel pathophysiological mechanisms of pericardial injury and constrictive pericarditis. World J Cardiol 2018;10:87‑96.
6. Lima NA, da Costa Lino DO, Coelho NM, Melgar T. Tuberculous constrictive pericarditis. BMJ case reports 2019;12.
7. Torio CM, Moore BJ. National inpatient hospital costs: The most expensive conditions by payer, 2013: Statistical brief #204. Healthcare Cost and Utilization Project (HCUP) Statistical Briefs. Rockville, MD: Agency for Healthcare Research and Quality; 2006.
8. Guelar A, Gatell JM, Verdejo J, Podzameczer D, Lozano L, Aznar E, et al. A prospective study of the risk of tuberculosis among HIV‑infected patients. AIDS 1993;7:1345‑9.
9. Selwyn PA, Hartel D, Lewis VA, Schoenbaum EE, Vermund SH, Klein RS, et al. A prospective study of the risk of tuberculosis among intravenous drug users with human immunodeficiency virus infection. N Engl J Med 1989;320:545‑50.
10. Lönroth K, Williams BG, Stadlin S, Jaramillo E, Dye C. Alcohol use as a risk factor for tuberculosis – A systematic review. BMC Public Health 2008;8:289.
11. Kamboj M, Sepkowitz KA. The risk of tuberculosis in patients with cancer. Clin Infect Dis 2006;42:1592‑5.
12. Baker MA, Lin HH, Chang HY, Murray MB. The risk of tuberculosis disease among persons with diabetes mellitus: A prospective cohort study. Clin Infect Dis 2012;54:818‑25.
13. Hussein MM, Mooij JM, Roujouleh H. Tuberculosis and chronic renal disease. Semin Dial 2003;16:38¬44.
14. Pien FD, Yoonszai BG, Pien BC. Mycobacterial infections in patients with chronic renal disease. Infect Dis Clin North Am 2001;15:851‑76.