Descriptive Epidemiological Analysis of Cestode Infections in Nevada: Characterizing Patients and Analyzing Trends using Patient Utilization Records, 2013-2019

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ABSTRACT

To understand the potential burden of human cestode infection, we utilized inpatient (IP), outpatient (OP), and emergency department (ED) discharge records from Nevada from 2013-2019. We found a total of 372 records of cestode parasitism. Most came from IP (50.3%) or OP (24.5%) visits. Diagnostically, *Taenia solium* taeniasis (30.9%) and central nervous system cysticercosis (38.4%) were most common, with comorbid organ involvement occurring in 7.8% of patients. IPs had a median stay of 3 days (range: 1-344), resulting in high total charges (median=$54,851). Patient race/ethnicity was predominantly Hispanic (49.5%) or white (32.0%); most were female (56.2%) and over the age of 40 (72.8%). There were no significant temporal trends (p=0.126), with an average of 53 (SD=9.9) cases per year. This analysis provides a case study for utilizing patient record databases as a means of indirect parasitic disease surveillance to obtain population-based estimates of parasite disease burden in a public health context in a state without mandated cestode parasite surveillance requirements.

KEYWORDS:
Cestoda; Cestodes; Zoonoses; Parasites; Cysticercosis; Parasite Surveillance

INTRODUCTION

Human parasitic diseases often do not garner the attention of the lay public, particularly in the United States (U.S.) where such diseases generally are less common or where sufficient and readily available treatments exist. However, studies suggest that parasitic infections represent a potentially significant health threat, especially among immigrants, many of whom are children (Herrick et al., 2020). Historically parasitic diseases were considered diseases of poverty, with most at-risk individuals associated with low economic status in developing countries. Hence, these diseases often were not afforded attention by the medical and public health communities in developed nations (Rosenfield et al., 1984). Fortunately, there has been some recognition that parasitic diseases, and neglected diseases in general, take a major medical and socioeconomic toll on society (Torgerson, 2013). These impacts are not just on human health, but also on animal health. Because many parasitic diseases of humans are also parasitic diseases of animals and livestock, the burden of zoonotic infections has led to the designation of addressing parasites from a One Health perspective. One Health recognizes the intimate relationships among the environment and both human and animal medicine and provides a context for addressing zoonotic diseases holistically (*One Health | CDC*, 2023).

Cestodes (i.e., tapeworms) are ubiquitous vertebrate parasites. Human cestode infections are common globally, but less is understood about cases in the United States (U.S.). Since there is irregular surveillance (i.e., there are few state mandates and no national mandates) for these parasites in the U.S., limited information is known about their public health impacts. There have been suggestions for public health surveillance of reportable parasitic diseases by the CDC and the WHO (*Developing Surveillance Indicators to Measure Global Progress against Pork Tapeworm*, n.d.), but, still, inadequate information is known about the burden of these diseases on human health globally. Further, unless a condition requires medical attention or results in significant disease, patients may never get tested or seek medical care, making it difficult to efficiently estimate disease burden and patient characteristics in the population. At the national level, cestode infections have been investigated most rigorously compared to other parasites, though not to our knowledge using recent data. From 2003-2012, for example, neurocysticercosis resulted in 18,584 hospitalizations totaling over $900,000 in total hospital charges, and from 1998-2011 an estimated 33,060 cysticercosis hospitalizations were found to result in 459 deaths (O'Keefe et al., 2015; O'Neal & Flecker, 2015)

Cestodes can enter the body in many ways, but most often this occurs through ingestion of eggs or, very rarely, proglottids (i.e., body segments) of the tapeworm, often inadvertently consumed with poorly prepared foods or through ingestion of intermediate invertebrate hosts (e.g., fleas or cockroaches). Once in the body, and depending on the species, development occurs through several stages until ultimately entering the digestive tract. Many cestodes in the intestines, for example, are often tolerated and may not cause demonstrable burden or may even go unnoticed. Unfortunately, however, extraintestinal tapeworm infections result in infection of the eye, liver, brain, or other organs and cause significant medical issues and significant morbidity and mortality (Bogitsh et al., 2019).

The primary aim of this study was to utilize a "Big Data" approach using medical discharge records as a potential source of data on cestode infections in Nevada over a seven-year period to understand the potential impact of these parasites on human health, and as a potential means of indirect public health surveillance that may be expanded to other parasitic diseases of importance. Analyzing large medical databases is of particular interest when attempting to understand the impacts of diseases that do not have state-level or national-level surveillance requirements.

MATERIALS AND METHODS

To understand the potential impact of both cestode infection of hosts (i.e., from *Echinococcus granulosis*, *Taenia* spp., *Hymenolepis nana*, and *Diphyllobothrium latum*) and extraintestinal infection (i.e., *Taenia solium* cysticercosis) on human health, we adopted a big data analytics approach utilizing secondary inpatient (IP), outpatient (OP), and emergency department (ED) discharge records from Nevada as a case study; the state is particularly useful as a case study owing to its status as a busy tourist destination with a growing immigrant population who may incidentally import parasites common in other parts of the world. The Center for Health Information Analysis (CHIA) for Nevada comprehensively collects administrative discharge records from all reporting hospitals and ambulatory surgical centers for the state (*CHIA*, n.d.). Part of the data that are collected include diagnostic codes (over 30 data fields for each patient record). Because the data sets were secondary, the UNLV IRB granted an exclusion to use the data for this project (UNLV IRB Protocol: 1482098-1). The CHIA data use agreement specifies that samples where n < 10 should not be exactly specified to preserve anonymity of the data; hence, we characterize data accordingly in the tabulated results.

We created a brute force algorithm to examine CHIA records and extract relevant International Classification of Disease (ICD) Codes from over 20 million patient records for both versions ICD 9 (utilized in the U.S. before 01 Oct 2015) and ICD 10 (utilized in the U.S. after 01 Oct 2015). For example, ICD 9 code 123.1 and ICD 10 code B69.0 both indicate cysticercosis (Table 1); a total of 60 codes related to cestode parasitism were utilized in this study. The algorithm proceeds thus: (1) read through each column of diagnostic codes and create a binary "0/1" indicator column for each cestode diagnosis (1 = cestode ICD code found); (2) sum across all newly created binary diagnostic columns (n = 33 columns); (3) create a binary indicator for discharge records in which the sum is not "0" in the summation column (this indicates that at least one diagnostic code of interest was found); and (4) extract all discharge records flagged as "1" (i.e., cestode code found). This algorithm results in a reduced data set containing only records of interest.

Table 1. International Classification of Disease (ICD) Codes used in this study.

Cestode Diagnostic Category	ICD 9*	ICD 10†
Echinococcosis	122.0-122.8	B67.0-B67.99
Taeniasis	123.0-123.3	B68.0-B68.9
Cysticercosis	123.1	B69.0-B69.9
Diphyllobothriasis	123.4	B70.0
Hymenolepiasis	123.6	B71.0
Dipylidiasis	123.8	B71.1
Other Cestode Infections	123.8-123.9	B71.8-B71.9

*ICD 9 codes were used in the U.S. for records before 01 October 2015 (i.e., through 2015, Q3)
†ICD 10 codes were used in the U.S. for dates after 01 October 2015 (i.e., beginning 2015, Q4)

We categorized discharge records by race/ethnicity, sex, and age for each data set (IP, OP, and ED). For categorical comparisons, we utilized chi-square analyses with exact p-values with a Bonferroni-adjusted post hoc tests if overall significance was found. Additionally, we summarized continuous variables for total charge and age for IP, OP, and ED as well as length of stay (LOS) for inpatient records. We utilized the Mann-Kendall test for trend with a bootstrapped p-value (n = 10,000 iterations) to examine potential monotonic temporal trends. All analyses were completed using SPSS (v. 28; IBM, Armonk, NY) and SAS (v. 9.4; SAS, Cary, NC).

RESULTS

Nearly 15,000 records of vector-borne and parasitic diseases were found, and 372 were cestode infections of varying types. There were significant differences among cestode OP visits compared to both IP an ED ($p < 0.001$). Diseases from *Diphyllobothrium* and *Hymenolepis* were present only in OP records. Most cases came from IP (50.3%), with a relatively equal percentage coming from OP (24.5%) or ED (25.3%) stays, though there was some variability among years, with OP stays notably increasing after 2015 (Figure 1). In terms of diagnoses, significant differences were found among discharge locations. Notably, taeniasis was significantly least common in the OP setting, and other cestode infections were significantly least common in IP settings (Table 2).

Figure 1. Nevada cestode patient records from IP, ED, and OP discharges shown as relative frequencies (cumulative bars; primary y-axis) and as total counts (dotted line; secondary y-axis) from 2013-2019.

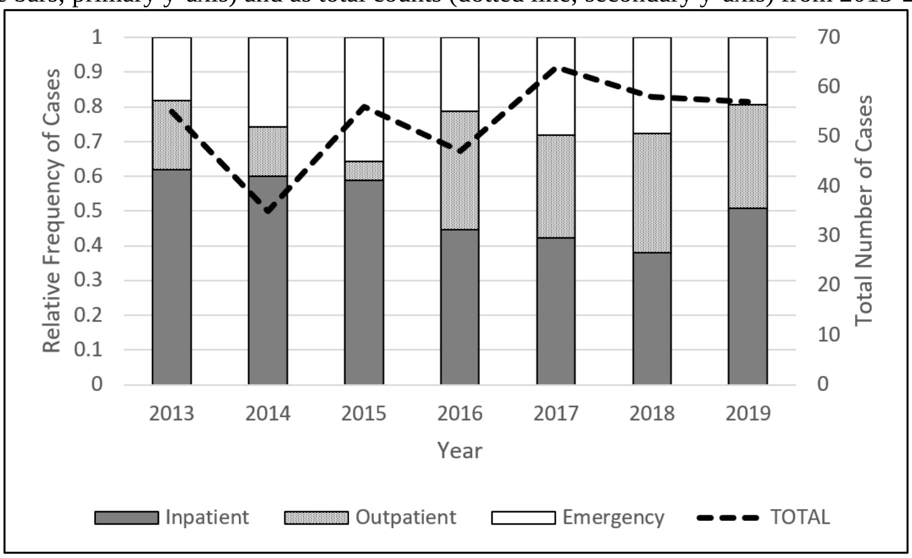

Table 2. Extraction disease details of cestode patient discharges within the IP, OP, and ED databases for ICD 9 and ICD 10 codes. The superscripts show Bonferroni adjusted post hoc tests comparing IP, OP, and ED.*

Cestode Diagnostic Category	**Inpatient No. (%)**	**Outpatient No. (%)**	**Emergency Department No. (%)**	**Chi-Square (p-value)**
Echinococcosis	19 (10.2)$_a$	14 (15.4)$_a$	< 10† (7.4)$_a$	
Taeniasis	68 (36.4)$_a$	17 (18.7)$_b$	37 (39.4)$_a$	
Cysticercosis	98 (52.4)$_a$	45 (49.5)$_a$	37 (39.4)$_a$	46.41 (< 0.001)
Diphyllobothriasis	< 10† (0)$_a$	< 10† (1.1)$_a$	< 10† (0)$_a$	
Hymenolepiasis	< 10† (0)$_a$	< 10† (4.4)$_b$	< 10† (0)$_a$	
Other Cestode Infections	< 10† (1.1)$_a$	10 (11)$_b$	13 (13.8)$_b$	

*Note that columns that do not share the same subscript differ significantly ($p < 0.05$).

†Data cells with fewer than 10 discharges are not exactly specified to preserve anonymity per CHIA data use guidelines.

Specific disease manifestations were noted in the analysis. Within all settings, cysticercosis of the central nervous system and *Taenia solium* taeniasis were the two most common diagnoses. In fact, these comprised 46.0% and 36.4% of the IP discharges, 35.2% and 16.5% of the OP discharges, and 26.6% and 34.0% of the ED discharges, respectively. An additional 26.6% of the ED discharges were unspecified cestode infections, and comorbid organ involvement (e.g., lung, bone, liver, etc.) occurred in 7.8% of all discharge records.

There were no statistical differences between sexes in the discharge data ($p = 0.152$). The race/ethnicity of patient discharge records differed significantly ($p < 0.001$) and were predominantly Hispanic (49.5%) or white (32.0%). OP discharges were statistically lower for Hispanics and significantly higher for whites. Age categories differed significantly as well ($p < 0.001$). In general, significantly higher rates were found for those 25+ years for IP discharges (Table 3).

Table 3. Categorical demographic characteristics of Cestode patient records within the IP, OP and ED databases. The superscripts show Bonferroni adjusted post hoc tests comparing IP, OP, and ED. *

Demographic Factor	Inpatient No. (%)	Outpatient No. (%)	Emergency Department No. (%)	Chi-Square (p-value)
Race/Ethnicity				
Black	< 10† (41.2) $_a$	< 10† (23.5) $_a$	< 10† (35.3) $_a$	58.0 (< 0.001)
Hispanic	115 (62.5) $_a$	24 (13.0) $_b$	45 (24.5) $_a$	
White	46 (38.7) $_a$	52 (43.7) $_b$	21 (17.6) $_a$	
Other/Unknown	19 (36.5) $_a$	11 (21.2) $_{a,b}$	22 (42.3) $_b$	
Sex				
Female	96 (51.4)	57 (62.6)	56 (59.6)	3.8 (0.152)
Male	91 (48.6)	34 (37.4)	38 (40.4)	
Age				
1-14	< 10† (33.3) $_a$	< 10† (33.3) $_a$	< 10† (33.3) $_a$	68.3 (< 0.001)
15-24	< 10† (22.2) $_a$	< 10† (33.3) $_a$	< 10† (44.4) $_a$	
25-39	29 (34.1) $_a$	28 (32.9) $_b$	28 (32.9) $_b$	
40-64	115 (57.2) $_a$	32 (15.9) $_b$	54 (26.9) $_a$	
65+	38 (55.9) $_a$	25 (36.8) $_a$	< 10† (7.4) $_b$	

*Note that columns that do not share the same subscript differ significantly ($p < 0.05$).
†Data cells with fewer than 10 discharges are not exactly specified to preserve anonymity per CHIA data use guidelines.

Costs associated with cestode diagnoses (represented as total charges in a visit) were quite variable, ranging from a low of $40 for an OP visit to over $2.7 million for an extended IP visit. Costs were often quite high for IP stays (med = $54,351) and are likely linked to relatively long hospitalizations for these patients (median = 3 days; range 1-344 days) (Table 4).

There was a noticeable temporal pattern in the number of total cases through time. However, this pattern did not represent a significant monotonic trend ($T_b = 0.429$, $p = 0.1258$), and should be considered preliminary given the short range of time (Figure 1).

Table 4. Cestode medical charges and continuous age demographics for IP, OP, and ED stays and LOS statistics for IP data.

Variable	Min	Max	Mean	SD	Median
Total Charge (US$)*					
Inpatient	4,527	2,768,199	116,376	231,616	54,851
Outpatient	40	66,946	4,632	9,745	1,226
Emergency Department	467	109,267	17,845	19,398	11,367
Age (in years by setting)					
Inpatient	8	90	53.0	16.59	52
Outpatient	12	90	50.1	20.60	50
Emergency	1	90	45.2	14.75	47.5
LOS (days)					
Inpatient	1	344	9.1	27.20	3

*Charges are rounded to nearest dollar value.

DISCUSSION

Cestode parasitism represents an important, but neglected, collection of diseases of public health importance. In fact, some have argued that among neglected tropical diseases, cestode infections are "neglected, neglected" diseases owing to lack of research (Budke et al., 2009). Though tapeworms and other parasites occasionally are the subject of popular literature (Desowitz, 1987; Zimmer, 2000), there is relatively little coverage of cestode disease burden in the U.S., and none, to our knowledge, for Nevada or that have utilized discharge data for analysis. Hence, this study represents an important, novel examination of tapeworm parasitic disease.

Diagnosis of cestode infection in this study demonstrated several interesting patterns. Cestode infections among Hispanics represented the largest number of diagnoses, with a high IP rate (62.5%). Given Nevada's large Hispanic population, and increasing immigrant community, imported tapeworm cases and other neglected diseases in this population are useful to consider (White & Atmar, 2002). Further, many infections were seen among older patients, many of whom were seen in the IP setting. Comorbidities among aging patients with chronic disease is well-documented (Fillenbaum et al., 2000); however, the addition of a potential parasitic burden to existing comorbidities is largely unknown. Further, results from this study suggest that cestode diagnoses are related to a high-cost burden, with median inpatient care exceeding $50,000 per patient. Clearly, further work is needed to understand these results in the context of public health.

Globally, cestode infections are much more commonly studied than in the U.S. In fact, it is estimated that cestode zoonotic diseases account for nearly 75% of global disability life years lost (Xiao et al., 2013). These authors also suggest that cestode parasitism is particularly burdensome in Asian countries, largely associated with dietary preferences (e.g., fish) that provide an avenue for infection (Scholz & Kuchta, 2016). Unfortunately, formal study of clinical helminthology in the U.S. has decreased, and relatively few training programs exist. In fact, parasitology education has largely been removed from medical microbiology training programs and medical schools in the U.S., leading to a gap in both diagnostic capabilities of treating physicians and in the study of rare, exotic tapeworm infections (Sapp & Bradbury, 2020). The inability to recognize cestode infections clinically is problematic and can lead to increased morbidity and mortality. Fortunately, clinical laboratory scientists are trained to recognize and diagnose common cestodes in North America (Mathison & Pritt, 2018); however, this assumes that clinicians can appropriately diagnose symptomatic disease. Perhaps laboratory study of model cestode organisms (Hemphill & Lundström-Stadelmann, 2021), may increase interest in parasitological basic-science inquiry that may eventually translate into clinical practice.

The results from this study suggest the presence of interesting patterns for future investigations. These results are hypothesis-generating and can be used for developing studies to further investigate why certain demographic groups may be more commonly represented in these data, and how this relates to the etiology of cestode infections. It can also be used in prevention of cestode infections through targeted community outreach by health educators. This study also highlights the actual disease and economic burden of infection by cestodes in the human population and provides useful information for assessing and treating these infections in IP, OP, and ED clinics where physicians may not have adequate training in parasitic diseases.

Medical records may assist in obtaining population-based estimates of parasitic disease burden in the population and provide useful additional data for underfunded public health surveillance programs; additionally, these records contain a rich resource of additional information beyond simple frequencies, including demographics, charges, medical procedures, comorbid conditions, and many other variables of potential interest in population health surveillance. An interesting, recent study of parasitic diseases suggests that parasitism can be misdiagnosed in patients, particularly among those with COVID-19 symptoms (Głuchowska et al., 2021). Examination of large databases, as was done in this study, will allow for such conjectures to be addressed in future investigations.

No study is completed without limitations, and that is true here as well. Discharge databases contain unidentified patient records, and hence may contain multiple accounts of some patients if they were to be seen for the same condition more than once; hence, results are about discharges, not individual patients, per se. However, the number of multiple discharge records for any individual patient in relation to the millions of available records suggests that only a small percentage of multiple case-counts likely exist in the database. Further, our intention was to address the total number of cases to assess overall healthcare burden, so repeating patients still provide useful information in this context. Additionally, we utilized all patient ICD codes, regardless of position, and therefore we did not focus only on primary diagnosis in this study. We believe that only using primary diagnoses may lead to undercounting disease burden. For example, since patients may seek treatment for symptoms (e.g., neurological issues) and are later found to have cestode CNS involvement, their primary diagnosis may be neurological; therefore, we used a comprehensive approach to extract all data with cestode ICD codes in this study.

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