Title
Examining the Relationships Among Neurocysticercosis, Presenting Symptoms, & Stroke

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Publication Date
2014

Peer reviewed|Thesis/dissertation

THE UNIVERSITY OF CALIFORNIA

LOS ANGELES

Examining the Relationships Among Neurocysticercosis, Presenting Symptoms, & Stroke

A dissertation submitted in partial satisfaction of the

requirements for the degree Doctor of Philosophy

in Nursing

by

Jennifer Ann Garland

2014

ABSTRACT OF THE DISSERTATION

Examining the Relationships

Among Neurocysticercosis, Presenting Symptoms, & Stroke

by

Jennifer Ann Garland

Doctor of Philosophy in Nursing

University of California, Los Angeles, 2014

Professor Wendie Robbins, Chair

Neurocysticercosis (NCC), a parasitic infection of the human central nervous system with the organism *Taenia solium* is an important, yet neglected, global public health problem causing preventable disability such as seizure and stroke in those infected. NCC symptoms vary widely, based upon the number and location of lesions, and can be difficult to identify and diagnose.

NCC is a reportable disease in Los Angeles County. However, there is limited understanding of NCC disease burden in Los Angeles County due to reporting barriers.

This dissertation is presented in three papers. The first paper examines case reporting and demographics of probable NCC cases identified in a Los Angeles community hospital through review of computerized tomography (CT) brain scan reports performed during 2012 that describe evidence of lesions highly suggestive of NCC infection. The study identified 303 probable NCC cases and found that 7 of the 11 cases reported to Los Angeles County Department of Public Health in 2012 were from the study site.

The second paper describes the presenting symptoms and mortality data of identified probable NCC cases. The study found that 3.9% of cases presented with seizure upon admission to the hospital and that death occurred in 3.9% of cases. The most common presenting symptom was headache (24.7%).

The third paper analyzes the rate of prior and acute stroke in the 303 probable NCC cases. The study found that 28.3% had evidence of prior stroke and 13.2% had evidence of acute stroke on CT brain scan performed during their admission to the hospital. NCC infection was also shown to be statistically significant as an independent risk factor for acute stroke when other known stroke risk factors were controlled for. The odds of acute stroke for probable NCC-infected persons were nearly 25 times that of noninfected NCC persons in this study.

The research presented here improves the understanding of NCC disease burden in Los Angeles County, demonstrates differences in NCC presenting symptoms, and demonstrates that NCC infection is an independent risk factor for acute stroke.

The dissertation of Jennifer Ann Garland is approved.

Frank Sorvillo

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Mary Ann Lewis

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University of California, Los Angeles

2014

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ACKNOWLEDGMENTS

I would like to thank White Memorial Medical Center and Dr. Antonio Liu for their support of this study.

I would like to thank Professor Wendie Robbins for her patience, encouragement, and faith in this project.

VITA

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CHAPTER 1: INTRODUCTION

Cysticercosis, an infection caused by a parasite called *Taenia solium (T. solium*), is a pork cestode (tapeworm) that creates cysts in different areas in the body. The *T. solium* organism is transmitted between pigs and humans through fecal-oral transmission, or from pigs to humans through eating undercooked pork. It is considered a zoonotic infection because *T. solium*'s complex life cycle involves pigs and humans.(1, 2) After the eggs are ingested, they pass through the lumen of the stomach and migrate to different parts of the body, very often to the brain, spinal cord, and eyes, where they form cysts and persist for years causing a wide range of clinical symptoms.(3)

Neurocysticercosis (NCC) is the most common helminth infection of the nervous system and is endemic in developing countries with poor sanitation and improper slaughterhouse practices.(4) It is endemic in Latin America where pigs are maintained as livestock and have access to human waste due to poor sanitation infrastructure. The infection is also prevalent in Sub-Saharan Africa and Asia.(5)

The World Health Organization (WHO) has classified cysticercosis as one of 17 neglected tropical diseases (NTD).(6) Roughly 90% of cysticercosis patients in the United States are immigrants from Latin America, and over half of the cysticercosis cases examined in a 2011 study focusing on nationwide cysticercosis mortality rates were found to be from Los Angeles County.(6-9)

No cases of cysticercosis or NCC were reported to LA County Department of Public Health during 2009 and 2010 by the community hospital in East Los Angeles

where data were collected for the studies described in this dissertation, despite the hospital serving an 89.8% Hispanic population, many of whom are immigrants from Latin America.(10, 11) This suggests there may be a significant problem of pervasive underreporting of this disease.(12)

Stroke syndromes have been identified in approximately 3%-12% of NCC cases.(13-15)Stroke incidence in the United States is 3.73 [95% confidence interval (CI), 3.51–3.96] per 1000 person-years for total stroke, 3.29 (95% CI, 3.08–3.50) per 1000 person-years for ischemic stroke, and 0.49 (95% CI, 0.41–0.57) per 1000 person-years for hemorrhagic stroke.(16)Stroke occurs when blood flow to a part of the brain stops due to a blood clot in the cerebral arteries (ischemic) or from a blood vessel in part of the brain becoming weak and bursting open (hemorrhagic).(17, 18) Stroke is the fourth leading cause of death in the United States and the leading cause of disability.(19) Symptoms of stroke depend on what area of the brain is damaged. Common symptoms include slurred speech, expressive or receptive aphasia, blurry vision, numbness or tingling on one side of the body, sudden headache, dizziness, weakness of one side of the body, and loss of coordination. Ischemic and hemorrhagic stroke are medical emergencies that require immediate attention. Permanent neurological damage occurs in both ischemic and hemorrhagic stroke without prompt medical attention.(17-20)

Although stroke has been known to occur in NCC patients, seizures are the most common (78.8%) presenting symptom associated with NCC,(1) and this association has overshadowed examination of NCC infection as a risk factor for stroke. The mechanism

of stroke in NCC cases is reported to be related to vascular and tissue inflammation in the area of the brain closest to the cysticerci lesion.(21) Based upon clinical observations in a primary stroke center, daily review of CT brain scans showed anecdotal evidence of NCC in stroke patients at a seemingly higher rate than that reported in the literature, strongly suggesting NCC as a greater risk factor for stroke than previously reported.(14)

Significance

Little is published on the relationship between NCC and stroke, and most of that research comes from Latin America, despite large Hispanic populations with high incidence of NCC in other parts of the world. One study from Ecuador, where NCC is endemic, identified a statistically significant association of NCC as a risk factor for stroke but did not quantify the strength of the association.(22) A recent review article reports that stroke syndromes are identified in about 3% of NCC patients.(14) Sotelo and colleagues reported an 11.8% incidence of ischemic stroke in NCC patients.(15) Incidence reporting for hemorrhagic stroke in NCC patients could not be found in the literature. Therefore, the purpose of this dissertation is to understand the relationship between NCC, presenting symptoms, and stroke prevalence, and to specifically measure the stroke prevalence in identified NCC cases during 2012 at a community hospital in Los Angelesthat serves a largely Hispanic population. The overlapping factors in the Hispanic population of increased risk for stroke in NCC and the high NCC rate suggest this is an area that needs further study.(13)

Specific Aims

In order to further describe the relationship between stroke and NCC, this dissertation research utilized retrospective review of hospital reports of all CT brain scans without contrast in adults ages 21 and over, conducted January 1, 2012 to December 31, 2012. The aims of this study were as follows:

1. Describe the proportion of individuals with CT brain scan evidence of presumptive NCC infection overall and across demographic and selected medical history characteristics.

   Hypothesis: There will be demographic and medical history differences between patients with and without evidence of NCC.

   Research question: How many individuals demonstrated evidence of probable NCC lesions on CT brain scan in 2012?

2. Compare the proportion of patients with CT brain scan evidence of NCC and presumptive stroke with what is reported in the literature for patients with stroke.

   Hypothesis: Because the urban community hospital is a Primary Stroke Center (PSC), serving a Latino and Hispanic immigrant population, we will see a higher proportion of NCC patients presenting with evidence of stroke than is reported in the literature in prior studies.

   Research question: Are the percentage of stroke patients identified within the probable NCC cases similar to or different from the reports in the literature?

3. Compare the presenting symptoms of patients with and without CT brain scan evidence of NCC across groups: Stroke (ischemic, hemorrhagic), Focal (transient ischemic), Other Neuro, Non-Neuro.

   Hypothesis: There will be differences in presenting symptoms across groupsfor those with and without evidence of NCC who have evidence of the following: (a) transient ischemic attack, (b) ischemic stroke, (c) hemorrhagic stroke, (d) focal, (e) other neuro and (f) non-neuro.

   Research question: What are the differences in presenting symptoms in patients with positive NCC lesions and those patients without NCC lesions?

4. Compare mortality at discharge for those positive and negative for CT brain scan evidence of NCC.

   Hypothesis: There will be differences in mortality rates across groups for those with and without evidence of NCC who have evidence of the following: (a) transient ischemic attack, (b) ischemic stroke, (c) hemorrhagic stroke, (d) focal, (e) other neuro and (e) non-neuro.

   Research question: What are the differences in mortality rates in patients with and without evidence of NCC?

Theoretical Framework

This study was based upon two theoretical frameworks. Rothman's *Epidemiological Model of Disease Causation* was chosen as one framework.(23) The model describes the complex interaction of host, agent, and environment in disease

transmission facilitation and often refers to infectious disease processes with a pathogenic agent. The morbidity surveillance pyramid is the second theoretical framework chosen for this dissertation. The morbidity surveillance pyramid is used to illustrate the availability of morbidity data at each surveillance level. With each ascending level, reported data availability shrinks and only a fraction of cases from the level below are captured.(24)For this study, the focus was on underreported patients who presented for treatment who were identified as probable NCC cases, but were not reported to the local health department within 7 days, as required by Title 17, California Code of Regulations (CCR), 2500.(25)

Methodology

This was a descriptive, comparative study utilizing retrospective review of all CT brain scan reports and images and associated patient medical records from January 1, 2012 to December 31, 2012 at a community hospital. The hospital, located in an urban setting in East Los Angeles, serves a primarily Hispanic/Latino population. CT brain scan reports and images were electronically available for review at the facility through Centris, a medical record database program. Data were analyzed utilizing descriptive statistics and logistic regression model analysis.

This dissertation consists of seven chapters. Chapter 2 reviews the literature and examines disease transmission of cysticercosis and NCC, and reviews stroke definitions, subtypes, and clinical risk factors associated with stroke examined in the dissertation study. Chapter 3 discusses the two theoretical frameworks upon which the study is based.

Chapter 4 describes the methodology, eligibility criteria, and operational definitions. Chapter 5, a manuscript, "Estimating the Under-reporting of Probable Neurocysticercosis Cases in a Community Hospital," was submitted to PLoS Neglected Tropical Diseases during July 2014 and is currently under review. The abstract has also been submitted to the 2014 International Meeting on Emerging Diseases and Surveillance, taking place in Vienna, Austria. This manuscript describes the results of 7,363 CT brain scans reviewed in 2012. Probable NCC cases were identified and compared to those reported to the Los Angeles County Department of Public Health Acute Communicable Disease Control Unit. Chapter 6, a manuscript, "Presenting Symptoms and Mortality of 303 Probable Neurocysticercosis Cases with Positive Radiographic Imaging in an East Los Angeles Hospital" was pre-submitted as an abstract to The American Journal of Tropical Medicine and Hygiene in April 2014 and invited for full manuscript submission. Chapter 7, a manuscript, "Presence of Probable Neurocysticercosis Infections Associated with Acute Stroke in a Los Angeles Community Hospital," was submitted in August 2014 as an abstract to the 2015 American Heart Association/American Stroke Association's (AHA/ASA) International Stroke Conference in Nashville, Tennessee. This manuscript describes the finding that probable NCC infection was an independent risk factor ($p<.001$) for acute CVA after controlling for associated clinical risk factors. The odds of acute stroke for probable NCC-infected persons were nearly 25 times that of non-NCC-infected persons in this study. This manuscript will be submitted to the American Heart Association/American Stroke Association's journal *Stroke*.

CHAPTER 2: LITERATURE REVIEW

This chapter discusses the current literature regarding what is known about cysticercosis, neurocysticercosis (NCC), the presenting symptoms of NCC, and stroke. NCC is a disease of many faces, with symptoms varying from person to person. No one size fits all. This literature review started with a PubMed search on cysticercosis/ neurocysticercosis, stroke, and stroke in NCC.

Disease Life Cycle

To aid in understanding the literature, a review of the life cycle of the tapeworm that causes NCC is presented. *Taenia solium* is a zoonotic cestode of the genus Taenia and has a complex, two-host life cycle (Figure 1). Humans are the only definitive host of the adult tapeworm; both humans and pigs can act as intermediary hosts, harboring the larve of cysticerci.(26)

The adult tapeworm has three main components, a scolex with four suckers and a rostellum, or double crown of hooks; a narrow neck; and a strobila formed by several hundred proglottids that measure 2-4 meters but can reach up to 10 meters (Figure 2).(3) The more distal proglottids of mature tapeworms are usually gravid with eggs and are frequently detached from the worm and expelled in the feces, disseminating 50,000-60,000 eggs per proglottid.(27)

Taeniasis

Taeniasis, the infection involving the parasite in the tapeworm (adult) stage, occurs only in the human host and is acquired by the ingestion of raw or poorly cooked

pork infected with T. solium cysts. Taeniasis is known to be a mild, mostly asymptomatic disease, and infected persons tend not to notice the passage of tapeworm segments in the feces, so they do not seek medical care.(15)

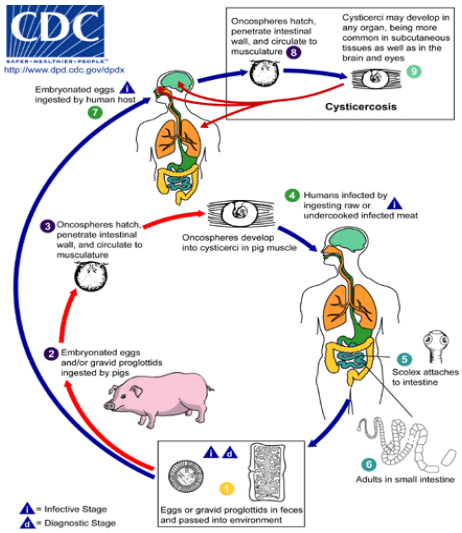

Figure 1.
Life Cycle *Taenia solium*.

The experiments of Kuchemaister in 1855 confirmed the link between taeniasis and cysticercosis and demonstrated that young tapeworms could be detected in autopsies from prisoners who were fed infected pork.(28) Viable T. solium cysts present in pork burrow into the small intestine after ingestion, and the scolex attaches to the intestinal mucosa with its suckers and hooks. The parasite then begins to form segments or proglottids until it reaches adult maturity around 2-3 months. During this time, the tapeworm causes little discomfort to the human host.(4)

In the adult form, the distal segments of the worm that are filled with eggs break off into the gastrointestinal tract and are shed in the stool of the host. If the host does not have access to indoor plumbing, the stool, filled with eggs, are disseminated into the environment and can reach either pigs when they rummage for food or humans by way of a contaminated water or food supply.(29) Poor infrastructure and the lack of access to

proper sanitation are pathogenic forces in the role of cysticercosis disease transmission.(30)

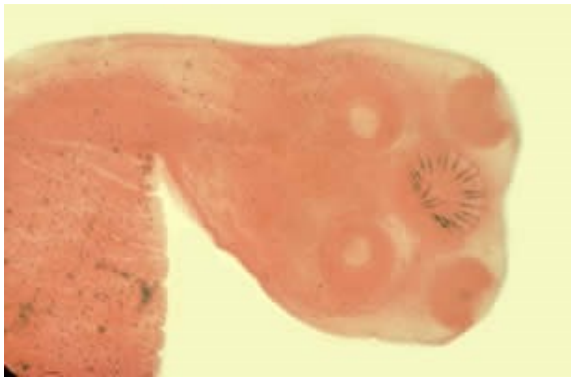

Figure 2.

Adult Tapeworm.

Cysticercosis

Cysticercosis is the infection involving the larval stage of the parasite *T. solium*,following the ingestion of viable eggs. Pigs, the intermediate host, are often infected with *T. solium* by direct ingestion of human feces, although exposure through contaminated water, soil, vegetables, or insects is also possible.(26) Humans are infected primarily by accidental ingestion of *Taenia* eggs through fecal-oral exposure. After ingestion, gastric acid helps to dissolve the eggs and liberate the embryos, which cross the intestinal mucosa and are then transported by the circulatory system to the liver and lungs.(3) It appears that a proportion of all embryos are cleared in the liver. The rest of the surviving parasites reach skeletal muscle, the brain, or other tissue, and in approximately three months, they develop into larval vesicles, also called cysts or cysticerci.(15) Cysts are most often found in muscle tissue, the eyes, and the brain, and can cause diverse clinical manifestations in humans, depending on their number, stage, and location, and the immune reaction of the host.(9) Seizures, one of its most apparent symptoms, tend to appear 3-5 years after exposure, after the degeneration and death of cysts.(1)Cysticercosis

in swine, however, rarely presents with clinical symptoms, even for massive infections. Pigs are slaughtered on average at 9-12 months of age, which is most likely before the cysts have had enough time to deteriorate and die.(29)

Clinical Presentation and Diagnostic Criteria

The clinical presentation of human cysticercosis depends on the number, size, location, and stage or viability of cysts, as well as the presence of inflammation.(5, 31) Considering all the possible combinations of these factors, it is not surprising that cysticercosis can present with virtually all neurological symptoms, thus complicating diagnosis of the disease.(32) NCC can cause both seizure and stroke. A recent review article described seizure as the most common presenting symptom in nearly 80% of NCC patients,(1) while another paper found that 11.8% of NCC cases demonstrate evidence of stroke.(15) The present study used Del Brutto's standardized diagnostic criteria for human cysticercosis as the clinical inclusion criteria (Table 1).(33)

Table 1

Diagnostic Criteria for Neurocysticercosis

(Del Brutto OH, et al, Neurology. 2001, with permission from American Academy of Neurology)
Absolute Criteria
Histological demonstration of the parasite from biopsy of a brain or spinal cord lesion
Evidence of cystic lesions showing the scolex or neuroimaging studies
Direct visualization of subretinal parasites by funduscopic examination
Major Criteria
Evidence of lesions highly suggestive of neurocysticercosis on neuroimaging studies
Positive serum immunoblot for the detection of anticysticercal antibodies
Resolution of intracranial cystic lesions after therapy with albendazole or praziquantel
Spontaneous resolution of small single-enhancing lesions
Minor Criteria
Evidence of lesions suggestive of neurocysticercosis on neuroimaging studies
Presence of clinical manifestations suggestive of neurocysticercosis
Positive CSF ELISA for detection of anticysticercal antibodies or cysticercal antigens
Evidence of cysticercosis outside the CNS
Epidemiological Criteria
Individuals coming from or living in an area where cysticercosis is endemic
History of frequent travel to disease-endemic areas
Evidence of a household contact with Taenia solium *infection*

DEGREES OF DIAGNOSTIC CERTAINTY
DEFINITIVE DIAGNOSIS
PRESENCE OF ONE ABSOLUTE CRITERION
PRESENCE OF TWO MAJOR PLUS ONE MINOR OR ONE EPIDEMIOLOGICAL CRITERIA
PROBABLE DIAGNOSIS
PRESENCE OF ONE MAJOR PLUS TWO MINOR CRITERIA
PRESENCE OF ONE MAJOR PLUS ONE MINOR AND ONE EPIDEMIOLOGICAL CRITERIA
PRESENCE OF THREE MINOR PLUS ONE EPIDEMIOLOGICAL CRITERIA

Diagnosis

The advent of neuroimaging techniques such as Computed Tomography have greatly improved NCC diagnosis. Such imaging techniques provide improved descriptions of the number, location, and size of brain lesions, as well as the presence and degree of inflammatory reactions.(34) Positive brain imaging is one of the three absolute criteria for NCC diagnosis.(33) The degenerative stages of cysticerci are classified into four stages: viable, colloidal, nodular-granular, and calcified.(35) Calcification of dead cysts show as small, punctuate hyperdense lesions. Multiple lesions are not uncommon, and they may present with cysts in different stages.(3, 36) This severe form of the infection, called intraparenchymal neurocysticercosis, is the most clinically relevant form of the disease. It accounts for up to 70% of all cases and presents with mainly epileptic seizures. Once the parasite enters the nervous system, cysticerci are protected by the blood-brain-barrier and remain viable primarily with perilesional inflammatory reaction.

The larvae then cause an inflammatory reaction in the surrounding brain tissue that may result in a seizure or a stroke.(37)

Treatment

Treatment of taeniasis aims at interrupting the chain of transmission, thus preventing future cases of human and swine cysticercosis, particularly within people and animals in close contact with the tapeworm carrier. Two antiparasitic drugs are primarily used, praziquantel and albendazole.(26) Antiseizure medications and corticosteroids are supplemental treatments, depending on the stage and form of disease. Surgical resection and ventricular peritoneal shunting are also possible treatment of the cysts.(38)

A recent review of the literature demonstrated that nearly 80% of symptomatic NCC cases had clinical manifestations of seizure/epilepsy, a disabling neurological disorder. An overwhelming amount of literature discusses seizure as the hallmark presenting symptom of NCC. In contrast, NCC is currently underrecognized as a cause of stroke, in spite of research indicating a significant link between the two. A recent review article reports that stroke syndromes are identified in about 3% of NCC patients.(39) Sotelo and colleagues reported an 11.8% incidence of ischemic stroke in NCC patients.(15) Stroke may cause significant disability and possibly death. Thus, the link between NCC infection and stroke warrants further study, as NCC patients are at an increased risk of stroke despite their lack of other cerebrovascular risk factors.(13) By increasing awareness, education, and prevention efforts to this target population, health professionals may be able to help patients prevent future infection and reduce the

incidence and disability for stroke and NCC through targeted education outreach. It is also imperative for neurologists to become familiar with this potential NCC complication.

Stroke

Stroke is a leading cause of disability, often rendering a person incapacitated and unproductive, and costing society roughly $54 billion dollars a year in days of lost work, cost of medications, and health care services.(18, 20) Stroke occurs when blood flow to a part of the brain stops due to a blood clot in the cerebral arteries (ischemic) or from a blood vessel in part of the brain becoming weak and bursting open (hemorrhagic).(40, 41) It is the fourth leading cause of death in the United States and the leading cause of disability.(42) Stroke symptoms depend on what area of the brain is damaged. Common symptoms include slurred speech, expressive or receptive aphasia, blurry vision, numbness or tingling on one side of the body, sudden headache, dizziness, weakness of one side of the body, and loss of coordination. Ischemic and hemorrhagic stroke are medical emergencies that require immediate attention. Permanent neurological damage occurs in both ischemic and hemorrhagic stroke without prompt medical attention.(43, 44)

One method for classifying stroke, developed for the Trial of Org 10172 in Acute Stroke Treatment (TOAST), utilizes probable stroke mechanisms to assign stroke subtypes. This stroke classification has been extensively validated and is utilized in both clinical research and general practice.(45) In this classification scheme, strokes are distinguished as resulting from (1) large artery atherosclerosis, (2) cardioembolism, (3)

small artery occlusion, (4) other causes, such as a disease process, or (5) undetermined or cryptogenic cause. Epidemiological studies demonstrate that a majority of strokes are ischemic in nature (87%), with the remainder being hemorrhagic (13%).(41)

Thrombolytic Treatment for Ischemic Stroke

Treatment for ischemic stroke is limited to thrombolytic therapy with intravenous (IV) tissue plasminogen activator (tPA) initiated within 4.5 hours of stroke onset. The Food and Drug Administration (FDA) currently recommends treatment with tPA for symptoms occurring within 3 hours. However, since 2009 the American Heart Association/American Stroke Association has recommended that tPA can be safely used within the first 4.5 hours in ischemic stroke patients meeting the clinical criteria. The mechanism of the medication dissolves the clot that has formed in the cerebral artery by dissolving the fibrin mesh holding the clot together. The medication offers a 30% chance of improvement and recovery, with a complication rate of 6%.(46)

Stroke in Hispanics

Stroke risk varies widely by race and ethnicity. Age-adjusted prevalence of stroke in the United States was 2.7% in 2006 and 2.6% in 2010.(45) The crude 3-year cumulative incidence (2000-2002) was 16.8 per 1000 in Mexican-Americans and 13.6 per 1,000 in non-Hispanic Whites. Mexican-Americans were observed to have a higher cumulative incidence of stroke at younger ages: 45-59 years had Relative Risk (RR) 2.04 (CI 1.55-2.69), and 60-74 years had RR 1.58 (CI 1.31-1.91). However, there was no difference between the two groups at $\geq$75 years of age. Mexican-Americans also

demonstrated higher cumulative incidences for intracranial hemorrhagic stroke and subarachnoid hemorrhagic stroke, even after adjusting for age.(46, 47)

Stroke in Women

Stroke is the fifth leading cause of death for men in the United States, but the third leading cause for women.(48) By 2030, there will be an estimated 72 million women >65 years of age, and women will increasingly outnumber men.(41, 42) These demographics suggest an anticipated increase in the burden of stroke in women. Some of this impact is explained by the fact that women live longer and therefore have a lifetime risk for stroke higher than men (20% versus 17%). In 2010, roughly 60% of stroke-related deaths in the United States occurred in women.

Clinical Risk Factors for Stroke

Aside from differences in ethnicity, sex, and age, there are also many established clinical risk factors known for increasing stroke risk. This study collected data on the 9 most commonly associated risk factors: (1) hypertension, (2) diabetes mellitus, (3) hyperlipidemia, (4) smoking, (5) atrial fibrillation, (6) depression, (7) carotid stenosis, (8) coronary artery disease, and (9) seizures.

Hypertension

Hypertension (HTN) or high blood pressure (BP) is a highly associated risk factor for stroke and affects men and women equally. Meta-analyses of large clinical trial data on antihypertensive therapy and related reduction of stroke show no difference between men and women.(42) Both sexes benefit significantly from antihypertensive treatment

and show a resulting 38% risk reduction in fatal and nonfatal cerebrovascular events in age groups >55 years of age.(43) Some studies suggest that positive responses to antihypertensive medication for blood pressure control are higher in women. However, high-risk elderly women >80 years of age using antihypertensive medication have not been successful in controlling their high blood pressure. The current American Heart Association/American Stroke Association recommendations for HTN treatment are the same for women and men.(48)

Diabetes mellitus

Diabetes mellitus (DM) is associated with a substantially increased risk for first ischemic stroke, with an adjusted RR range of 1.5 to 3.7. On a population level, DM may be responsible for >8% of first ischemic strokes.(47) Up to 28% of patients with ischemic stroke have pre-DM, and 25% to 45% have overt DM.(44)Disorders of glucose metabolism are also highly prevalent among patients with established cerebrovascular disease, a risk factor for ischemic stroke.

Hyperlipidemia

Hyperlipidemia (HLD), an associated risk factor for ischemic stroke and heart attack, contributes to increased risk by causing plaque buildup in the arteries. Statin therapy with intensive lipid-lowering effects is recommended to reduce risk of stroke and cardiovascular events among patients with ischemic stroke or TIA presumed to be of atherosclerotic origin.(47)

Smoking

Smoking is an important independent risk factor for ischemic stroke and contributes to increased risk of silent, asymptomatic stroke. Smoking substantially increases risk for stroke recurrence in the elderly. Recent research has also shown second-hand smoke to be associated with increased risk for ischemic stroke.(43) A recent population study examining over 30,000 patients demonstrated that the hazard ratio (HR) for stroke was increased by 2.05 (CI 1.68 – CI 2.49) for smokers.(49)

Atrial Fibrillation

Atrial Fibrillation (AF or A-fib) is the most common cardiac dysrythmia and is a modifiable risk factor for stroke. A-fib increases the risk of ischemic stroke 4-5 fold and is associated with high rates of mortality and disability. Stroke is the most dreaded complication of A-Fib. The overall number of men and women with A-fib is equal. Whites carry the highest prevalence of A-Fib compared to African-Americans, Hispanics, and Asians. The attributable risk for stroke due to A-Fib increases with age.(18) A-fib is treatable with anticoagulation therapy, such as warfarin, to reduce the risk of ischemic stroke.

Depression

Depression is a well-recognized consequence of stroke. However, in a large case-control study examining stroke participants in 22 countries, it was also shown to be a risk factor for stroke. The study found that participants who reported feeling sad, depressed,

or blue for > 2 weeks during the last 12 months were associated with a 35% increased odds of stroke, after adjustment for age and sex.(43)

Carotid Stenosis

Carotid stenosis occurs when ≥70% of the internal or external carotid arteries are blocked, and may involve symptoms of transient ischemic attack. Stenosis of the carotid blood vessels reduces oxygen supply to the brain and can result in a stroke. Treatment for carotid stenosis includes carotid artery stenting (CAS) or carotid endartarectomy (CEA), which is surgical reopening of the carotid vessels.(44)

Coronary Artery Disease

History of coronary artery disease such as myocardial infarction (MI) is associated with ischemic stroke. However, treatment of the disease can reduce incidence of stroke. A randomized control trial that followed MI patients for 4 years looked at death and thromboembolic stroke outcomes for MI treated with warfarin versus MI left untreated. The outcome of stroke was reduced by 19% in the warfarin group.(45)

Seizure

Similar to depression, seizure is a well-established consequence of stroke, particularly intracranial hemorrhage.(50) Seizure has also been shown to be a risk factor for stroke. In a large epidemiological study examining stroke comorbidity in epileptic patients, 24.2% of epileptic male patients were comorbid for stroke (both ischemic and hemorrhagic), versus 4.1% in the nonepileptic males. In female epileptic patients, 20.9% were comorbid for stroke versus 3.7% in nonepileptic females. (51)

CHAPTER 3: THEORETICAL FRAMEWORK

Epidemiological Model of Disease Causation

The *Epidemiological Model of Disease Causation,* as described by Rothman, was chosen as one of the theoretical frameworks for this study.(23) This model outlines the complex interaction of host, agent, and environment in disease transmission facilitation and describes the three conditions that must be met for NCC infection to be endemic: (1) sanitation is poor (agent is available), (2) pork consumption occurs (by the human host), and (3) pigs have access to human feces (in the environment).(52)

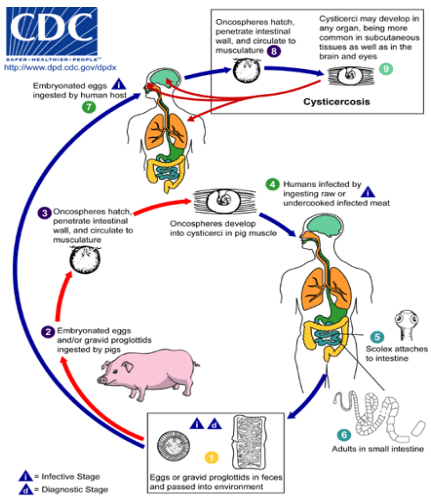

Figure 3.
Life Cycle *Taenia solium*.

These concepts are important to understand when planning prevention strategies at the primary, secondary, and tertiary levels. The model refers to infectious disease processes with a pathogenic agent.(23, 53) For example, in cysticercosis infection, pigs serve as intermediate hosts of the agent *T. solium*to continue the life cycle, while humans serve as definitive hosts.(54, 55) Developing countries are the usual environment for cysticercosis/NCC infection transmission, although the infection is being transmitted more frequently in the United States due to the immigration of asymptomatic taeniasis carriers (Figure 3).(9)

When examining the animal and human hosts in both developed and undeveloped infrastructure settings, the triad of agent, host, and environment interaction is applied to the model (Figures 4-9). The combination of all three elements and other associated risk factors must be present for disease transmission to occur; conversely, acquisition of the disease through exposure may be prevented if modification occurs in any or all of the host, agent, or environment (Figure 6).

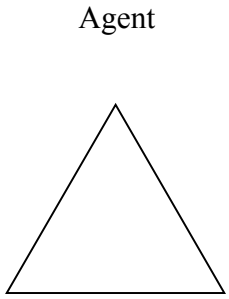

Figure 4.

Agent-Host-Environment.

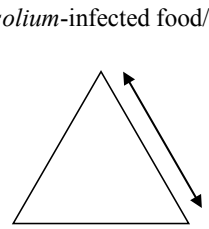

Figure 5.

Epidemiological Model of Disease Causation applied to cysticercosis in developing countries: pig host.

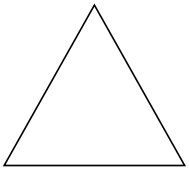

Figure 6.

Epidemiological Model of Disease Causation applied to cysticercosis in developed countries: pig host. In this model of disease, the agent-host-environment transmission links are broken because pigs do not have access to *t.solium*-contaminated food, water, or human waste, all of which serve as vehicles for the organism that perpetuates the life cycle of cysticercosis.(54, 55)

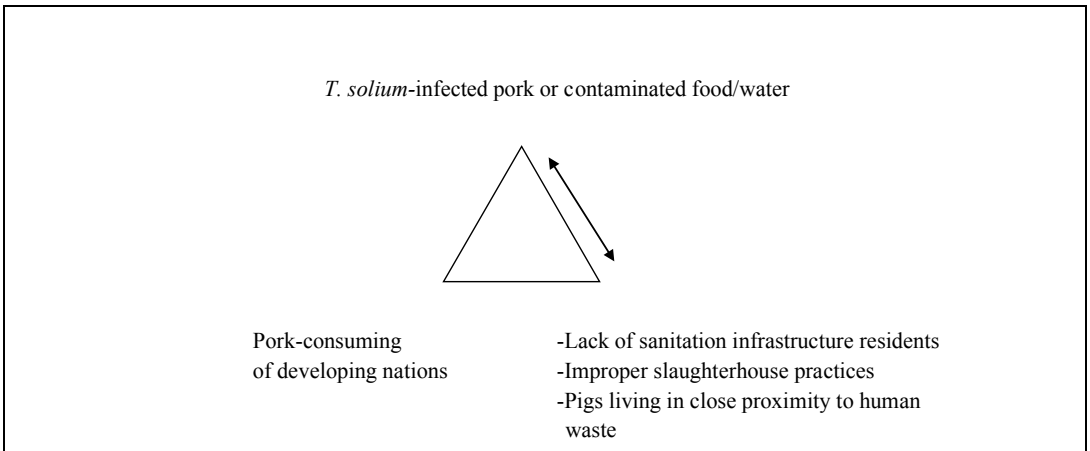

Figure 7.

Epidemiological Model of Disease Causation applied to cysticercosis in developing countries: human host.

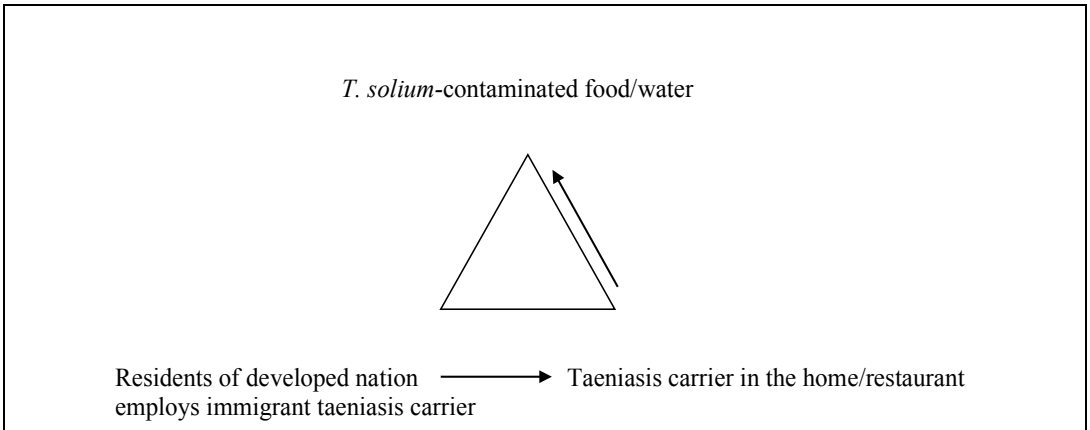

Figure 8.

Epidemiological Model of Disease Causation applied to cysticercosis in local transmission: human host.

Figure 9.

Process of Kitchen Transmission of Cysticercosis in Local Transmission: human host.

Figure 9 describes the dynamic of kitchen transmission that occurs in local transmission of cysticercosis. This dynamic has been demonstrated in local transmission of four NCC cases from 1990-1991 in an Orthodox Jewish Community in New York City.(27)

Morbidity Surveillance Pyramid

The second theoretical framework chosen for this dissertation is the morbidity surveillance pyramid (Figure 10).(24) This framework was chosen due to the barriers with reporting that were anticipated with the probable NCC cases identified in the study. Reliable and efficient disease reporting/notification systems are crucial for monitoring disease outbreaks and public health trends. These reporting systems also serve as the foundation of information that allows public health decision makers to make sound decisions when allocating health care resources and prioritizing public health policies

affecting communicable disease intervention.(56) In spite of the importance of such systems, there are gaps in disease surveillance procedures, disease reporting, and disease notification systems.(57) Many systems are impacted by a certain level of underestimation, leading to uncertainty regarding the actual incidence of a disease. Infectious diseases, specifically, are susceptible to underestimation because of their minor, self-limiting, or asymptomatic clinical presentations. Underreporting can occur as a result of underdiagnosis or misdiagnosis.(24, 56, 57) This study focused on underreported patients who presented for treatment and were identified as a probable NCC case, but were not reported to the local health department within 7 days, as required by Title 17, California Code of Regulations (CCR), 2500.(25)

The morbidity surveillance pyramid demonstrates the passive surveillance system process. In order for an NCC case to be reported, it must pass through the following process: a person becomes ill and presents to a primary care provider, the provider orders a CT brain scan, the radiologist reports the suspected infection to infection control, the infection control department reports the infection to the local health department, and finally, the local health department reports the infection to the state health department.(58) With each escalating level, information becomes scarcer and only a fraction of cases from the previous level are captured. If any step in this complex process fails to occur, cysticercosis/NCC infection is not reported.(24)

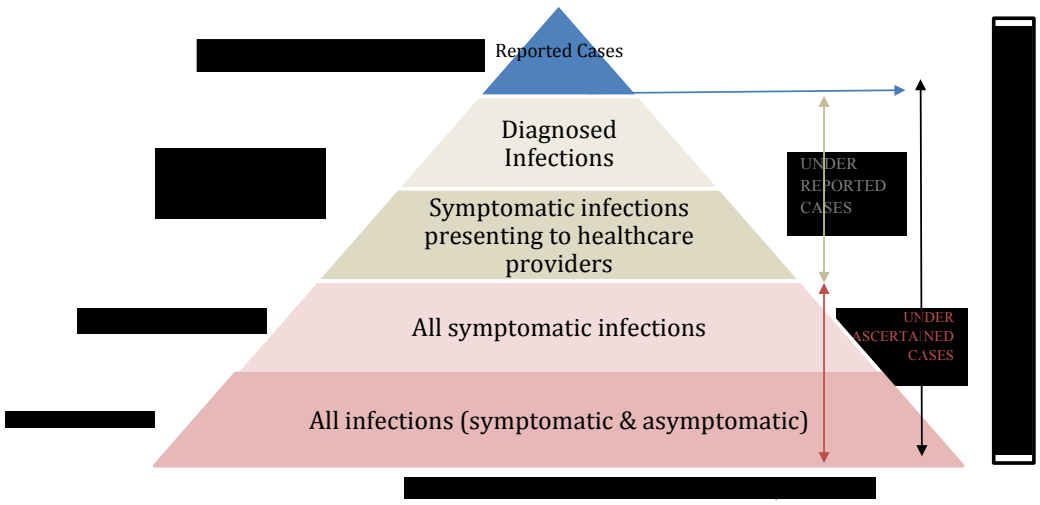

Figure 10.

Morbidity Surveillance Pyramid.

CHAPTER 4: METHODOLOGY

This was a descriptive, comparative study utilizing retrospective review of all noncontrast Computed Tomography (CT) brain scan reports and images and associated patient medical records from January 1, 2012 to December 31, 2012 at an urban community hospital. The hospital is located in an urban setting in East Los Angeles serving a primarily Hispanic/Latino population. This study compared individuals with and without NCC infection. CT brain scan reports and images were electronically available for review at the facility through Centris, a medical record database program. Associated hospital medical records were electronically reviewed in PowerChart. Institutional Review Board (IRB) approval was requested from the study institution and the South Campus General IRB, University of California at Los Angeles (UCLA), and approved in June 2013 (Appendices A & B).

Description of Study Population: Eligibility Criteria

This retrospective record review included CT brain scan (without contrast) reports conducted on all individuals over the age of 21 years admitted to the study facility from January 1, 2012 to December 31, 2012. Hospital medical records were also reviewed for demographic data, previous medical history of nine clinical risk factors (described in Chapter 2), and death disposition (Appendix C).

The CT brain scan reports were reviewed to identify evidence of presumed cysticercosis and/or neurocysticercosis (NCC) patients per radiology reports and categorized into two groups: (1) all patients with evidence of cysticercosis and/or NCC in

CT brain scan reports, and (2) all patients with evidence of acute ischemic or hemorrhagic stroke without cysticercosis and/or NCC.

Definition of cases consisted of CT brain scan reports with terminology identifying presence of cysticercosis or NCC, for example, "[abnormality] consistent with old cysticercosis" "[abnormality] likely related to old cysticercosis."

After identifying cases of presumed cysticercosis and NCC per radiology reports, patients were categorized into four groups: (1) Stroke, (2) Focal (Non-Stroke), (3) Other Neuro, and (4) Non-Neuro/Nonfocal, based upon presenting symptoms.

The category of *Stroke*included patients with evidence of lacunar infarcts and current or prior evidence of ischemic or hemorrhagic infarcts on noncontrast CT brain scan reports, as described by the interpreting radiologist, regardless of indication. Patients categorized as *Stroke*were further subcategorized as *Ischemic Stroke* or *HemorrhagicStroke*.

The category of *Focal Non-Stroke* included patients with noncontrast CT brain scans performed for brain, spinal cord, or nerve dysfunction that resulted in neurological deficits, such as loss of vision, seizure, aphasia, amnesia, slurred speech, and weakness or numbness in one part of the body, that suggest a specific part of the brain or nervous system is disrupted. This category of patients did not have evidence of previous or current lacunar, ischemic, or hemorrhagic infarcts on their noncontrast CT brain scan reports. Patients categorized as *Focal (Non-Stroke)* were further subcategorized as *Transient Ischemic Attack (TIA)* or *Non-TIA*.

The category of *Other Neuro (Non-Focal)* included patients with noncontrast CT brain scans performed for nonspecific indications, such as altered loss of consciousness, generalized weakness, headaches, confusion, and lethargy. These symptoms do not indicate that a specific part of the brain or nervous system is disrupted.

The final category, *Non-Neuro/Nonfocal*,included patients with noncontrast CT brain scans performed for other indications, such as motor vehicle accidents and falls, unrelated to spontaneous physiological onset of neurological symptoms.

Operational Definitions

For the purpose of this study, the following terms were defined:

Cysticercosis: an infection by the parasite *Taeniasolium* (*T. solium*), a pork tapeworm that creates cysts in different areas in the body.(4)

Neurocysticercosis: an infection by the parasite *Taeniasolium* (*T. solium*), a pork tapeworm that creates cysts involving the central nervous system and the eye.(59)

Ischemic stroke: occurs when blood flow to a part of the brain stops, usually from a blood clot.(20) Symptoms of stroke depend on what part of the brain is damaged. Prompt medical attention can save lives and reduce stroke disability. Permanent damage occurs in ischemic stroke.

Hemorrhagic stroke: occurs when a blood vessel in part of the brain becomes weak and bursts open, causing blood to leak into the brain. Some individuals have defects in the blood vessels of the brain, such as arteriovenous malformation (AVM) and aneurysm, that make this more likely. Acute hemorrhagic stroke is a medical emergency

and requires immediate attention. Permanent neurological damage occurs in acute hemorrhagic stroke.(17)

Transient ischemic attack (TIA): an episode when blood flow to a part of the brain stops for a brief period of time. A person will have stroke-like symptoms, but the blood flow resumes normally and symptoms resolve within 24 hours. Some sources are redefining the time for symptoms to resolve down to one hour. In a TIA, no permanent neurological damage occurs.(17)

Focal deficit: a specific area in which normal function is not present. An example is inability to feel sensation in a particular part of the body during a transient ischemic attack (TIA). A person may also have a focal deficit without having a TIA. An example of this is a Bell's Palsy, where an individual has an injury to cranial nerve III and appears to have a facial droop but has not had a stroke or a TIA. The reason for Bell's Palsy is unknown, but the suspected cause is a viral infection.(20)

Mortality rate: the ratio of deaths in an area to the population of that area.

Statistical Analysis

Univariate analysis was used to describe study population characteristics. Logistic regression was used to determine the differences between groups positive or negative for probable NCC on demographic and medical history variables (Aims 1-3) as well as the subgroups of stroke and nonstroke. Logistic regression is most appropriate for this study because the aim is to compare the non-NCC group to the NCC group and to compare the stroke to the nonstroke group. Comparisons to the published literature are described but

not compared statistically (Aim 2), as were the deaths at discharge due to small numbers (Aim 4).

Power Analysis

The sample size for this dissertation was constrained to the number of reports of all CT brain scans without contrast conducted for the time period January 1, 2012 to December 31, 2012 at the hospital from which the sample is drawn that are available, can be linked to patient records, and are from a patient that is 21 years or older. Based on the expected sample size of at least 122 cases of NCC, there will be a power of 0.80 to detect a large effect size of 0.612 at a p value of 0.001 when assuming a goodness of fit. A sample size of 22 strokes with NCC was needed for a large effect size of 0.6 at a p value of 0.001 and a power of 0.80 to examine the subcategory of stroke when assuming a goodness of fit.(60) To account for missing data, this investigator decided to oversample, collecting data on 303 probable cases identified during the 2012 study period. There were 40 acute strokes identified in the probable NCC group and 86 previous strokes identified in the probable NCC group.

Data Collection

Data were entered into an Excel spreadsheet by Collaborative Institution Training Initiative (CITI)-trained data abstractors, as required by the University of California South Campus General Institutional Review Board (IRB) and the Study Site AuthorizationAgreement. The data were de-identified prior to entry, and computers were maintained in a locked office. Data were coded prior to statistical analysis using SAS

statistical package Version 9.2 (SAS Institute, Inc, Cary, NC). The investigator re-abstracted approximately 10% of cases to ensure inter-rater reliability (Appendices A and C).

Inclusion of Women

The same parasite responsible for cysticercosis, *Taenia solium*, affects men and women equally. However, there is evidence that greater inflammation is observed in women who have cysticeri in their brain parenchyma.(61) A 2009 review of California NCC cases found that those with NCC were slightly more likely to be male than female (men 57.6%, women 42.4%).(32) As a result, women were expected to comprise at least 40% of the sample size. The study found women to comprise 68.9% of the 303 identified probable NCC cases**.**

Inclusion of Children

Very few children are diagnosed with NCC and typically do not experience ischemic or spontaneous hemorrhagic strokes at less than 21 years of age.(9) While children, defined by the NIH as a person less than 21 years of age, were not excluded from the study, it was expected that children would comprise < 1% of patient participants. One probable NCC case identified in the study was 20 years of age and comprised 0.3% of the study sample.

Inclusion of Minorities

Approximately 89.9% of the urban community hospital's Emergency Department encounters are with Hispanic patients.(10) In a review of NCC cases in California

performed in 2009, 84.9% of all cases were Latino.(32) It was expected that at least 89% of NCC cases identified in the study would be Latino or Hispanic; the resulting probable NCC cases identified in the study were 91.4% Hispanic, of which 68.9% were born in Mexico.

Limitations

All NCC cases identified were probable cases and not definitive, as defined by Del Brutto's 2011 *Diagnostic Criteria for Neurocysticercosis*.(33) It is possible that multiple cases of NCC were missed due to the radiologist's not specifying calcification origins on CT brain scan reports and the underestimation of NCC disease. Since this study was based on hospital record review, Berkson selection bias is a concern. Such bias occurs in hospital-based studies, which fail to include patients who might otherwise meet inclusion criteria but did not present for medical treatment. As a result, the study findings may not be applicable to NCC patients who did not present for medical treatment.(62) Another limitation is that the study did not analyze risks for exposure, making it difficult to assess the length of time and stage of infection of the probable NCC cases.

CHAPTER 5: ESTIMATING THE UNDERREPORTING OF PROBABLE NEUROCYSTICERCOSIS (NCC) CASES THROUGH ACTIVE CASE FINDING IN AN EAST LOS ANGELES HOPSITAL

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Manuscript word count: 2,458 **Tables**: 5 **Figures:** 3 **References:** 31

Keywords: *Taenia solium*, cysticercosis, demographics, neurocysticercosis, disease reporting, disease surveillance, case finding

Abstract

Objective: To investigate case reporting of probable neurocysticercosis (NCC) infection identified by CT brain scan reports and additional probable diagnostic criteria in the hospital medical record.

Design: A descriptive study was conducted utilizing retrospective review of 7,363 CT brain scan reports and associated patient medical records from January 1, 2012 to December 31, 2012 in a community hospital in East Los Angeles. To meet the definition of probable NCC, the case must have a CT brain scan report showing evidence of lesions highly suggestive of NCC and supporting epidemiologic features defined by the 2001 Diagnostic Criteria for Neurocysticercosis.(33) Cases of probable NCC identified through research review of records were compared to 2012 hospital discharge records (International Classification of Diseases) ICD-9 code 123.1 and Los Angeles County Department of Public Health's Acute Communicable Disease Control 2012 Annual Morbidity Report.

Results: Of the 7,363 CT brain scans reviewed in 2012, 303 (4.1%) patients met criteria for the diagnosis of a probable NCC case. Hospital ICD-9 123.1 discharge records for the same time period showed 17 newly identified cysticercosis cases. For this same time period (2012), Los Angeles County Department of Public Health's Acute Communicable Disease Control had 11 cysticercosis cases reported to them within LA County, and 7 cases were reported by the study hospital.

Conclusions: NCC is vastly underreported at this urban hospital. Study findings suggest an important role for active case surveillance triggered by CT brain scan report review coupled with medical record review for case identification.

Significance: This paper improves understanding of the extent of NCC disease burden and underreporting in Los Angeles County and provides evidence of the need for active NCC surveillance in hospitals serving large Hispanic populations.

Abstract word count: 285

Introduction

Cysticercosis is an infection caused by a parasite called *Taenia solium* (*T. solium*), a pork tapeworm that creates cysts in different areas in the body. Neurocysticercosis (NCC) is the same infection with the encysted larvae of the tapeworm located in the brain, eyes, and spinal cord and is the most common parasitic disease of the human central nervous system.(4) The *T. solium* organism is transmitted between humans and pigs, usually through eating undercooked pork or through fecal-oral transmission of food contaminated with eggs.(1) After the human ingests the eggs, they pass through the lumen of the stomach and migrate to different parts of the body, very often the brain, spinal cord, and eyes, where they form cysts and persist for years, causing varied and nonspecific clinical presentation such as headaches, seizures, and focal neurological deficits.(39)

NCC is endemic in developing countries with poor sanitation and improper slaughterhouse practices,(63)and is classified by the World Health Organization (WHO) as one of 17 neglected tropical disease (NTD) and subcategorized as one of eight endemic "neglected zoonotic diseases."(2) Although cysticercosis and NCC are often associated with being endemic to regions such as Latin America, more recent reports have identified a steady increase in the number of cases acquired in the United States due to contaminated food or water from a human tapeworm carrier.(7-9, 27, 64) Roughly 90% of cysticercosis patients in the United States are immigrants from Latin America,(4) and nearly half of the cysticercosis cases examined in a 2011 study focusing on

nationwide cysticercosis mortality rates were found to be from Los Angeles County.(7) With the introduction of noninvasive brain imaging, NCCis more frequently being found in asymptomatic cases.(27)

NCC is classified depending upon disease stage and location. The most common locations for NCC lesions to be found are the subarachnoid spaces and adjacent meninges, followed by the parenchymal form often seen by the gray matter and white matter junction.(34) NCC can lead to long-term disability, is the leading cause of acquired seizure disorder, and may result in death.(26) There is limited understanding of the burden of cysticercosis in the United States due to the disease being reportable in only five states, namely California, Texas, New Mexico, Arizona, and Oregon.(65) Prior studies have shown Southern California to be a location containing a significant majority of cases identified across the nation. However, due to unreliable reporting, the actual burden of cysticercosis and NCC cases in the United States and in Los Angeles County is unknown.(7, 66)

Reliable and efficient disease reporting/notification systems are crucial for monitoring disease outbreaks and public health trends. These reporting systems also serve as the foundation for information that allows public health decision makers to make sound decisions when allocating health care resources and prioritizing public health policies affecting communicable disease intervention.(56) Many systems are understood to be impacted by a certain level of underestimation, leading to uncertainty regarding the actual incidence of a disease. Some infectious diseases are susceptible to underestimation

because of their minor, self-limiting, or asymptomatic clinical presentations, and underreporting can occur as a result of underdiagnosis or misdiagnosis.(24) For this current study, the focus was on hospital reporting of patients who presented for treatment for medical conditions other than cysticercosis or NCC but were identified as comorbid for probable NCC, based on CT brain scan and additional probable diagnosis criteria in the hospital medical record. Title 17, California Code of Regulations (CCR), 2500 requires that all new cases of probable cysticercosis and NCC be reported to the local health department within 7 days of ascertainment.(25)

Methods

The research was conducted at a 373-bed urban community hospital in East Los Angeles that provides care for indigent patients in Los Angeles County. The hospital patient population comprises over 89.5% Hispanic individuals, with many patients immigrating from Mexico and Central America.(10) The study received approval by the UCLA Institutional Review Board (IRB) and the Western Institutional Review Board (WIRB), with a waiver of consent granted for the retrospective record review. All patient data collected for the study were de-identified according to IRB guidelines.

In 2012, the hospital conducted Computed Tomography (CT) brain studies for 7,363 patients (Figure 11). Probable NCC cases (as defined by Del Brutto and colleagues, 2001)(33) were identified utilizing retrospective review of all CT brain scan reports in the hospital Centris Enterprise Web V3.0 that were recorded from January 1, 2012 to December 31, 2012 and met additional criteria based on medical record review for the

diagnosis of a probable case (Table 2).(33) The following descriptors on brain CT scan reports were triggers to identify probable cases: large calcification consistent with old cysticercosis; probable old neurocysticercosis infection; neurocysticercosis; scattered calcifications highly consistentwith neurocysticercosis; punctuate calcifications consistent with neurocysticercosis; multiple large calcifications indicating oldcysticercosis infection; scattered, punctuate parenchymal calcifications consistent with neurocysticercosis; calcified lesions indicating probable cysticercosis; and other variations of these statements that included the term cysticercosis.

Associated patient medical records were reviewed in PowerChart to verify that minor criteria and/or epidemiological diagnostic criteria were met when probable NCC was reported on a CT brain scan (Table 2).(33) These criteria included clinical manifestations that were consistent with NCC infection such as seizure, headache, stroke symptoms, and places of birth where NCC is endemic, such as Mexico or Latin America.

Results

Of the total 7,363 CT brain scan reports reviewed, 303 (4.1%) scans showed evidence of probable NCC (Figure 12). These data were then compared to the study hospital's 2012ICD-9 123.1 discharge records that showed a case list of 17 primary diagnoses of cysticercosis for this same time period. There is not currently a separate ICD-9 code for NCC. Eleven of these 17 cases of cysticercosis were also identified during the research review of CT brain scans, giving a 68.75% recapture rate when comparing the two separate data sets. The remaining six cysticercosis cases that were

identified by the hospital ICD-9 coding, but not by the study, either did not receive a CT brain scan performed during hospitalization (2/17, 11.7%), or were scanned and the report was negative (4/17, 23.5%). These 4 patients with negative CT brain scans did have evidence of the infection in their medical record, resulting in the diagnosis (Table 4). TheLos Angeles County Department of Public Health's Acute Communicable Disease Control Annual Morbidity Report for 2013showed data from 2012 indicating the study hospital reported 7 existing cysticercosis cases for the year.(11) Total cases of cysticersosis and NCC reported to the health department county-wide totaled 11 in 2012. The study site reported 2.3% (7/303) of identified NCC cases to LAC DPH, comprising 63.6% (7/11) of the total cases reported for follow-up in Los Angeles County. At this time, no confirmatory testing information is available for the 11 reported cases.

Of probable cases identified, 68.9% (209/303) were born in Mexico, 13.5% (41/303) were born in the United States, and 6.9% (21/303) were born in Central or South America. Females comprised 66.9% of cases (203/303), and 33% of cases (100/303) were male. The probable cases ranged in age from 20 to 91 years, with a mean age of 64.7 years. Over 40% of probable cases were between the ages of 61-80 years old (125/303, 41.2%). Religion of probable cases was examined, and 2 of the 303 cases identified as Seventh Day Adventists, a non-pork consuming religion (Table 3).

Nearly all of the probable NCC cases (94%, 285/303) were seen in the ED, and just over half (52.4%, 159/303) of those cases were admitted to the hospital. The average length of stay for these 159 admitted cases was 4.5 days. Ten radiologists were identified

as interpreting CT brain scans conducted during the study period. However, only 9 of these radiologists reported lesions consistent with cysticercosis (Figure 13, Table 6). Payment type was examined and showed that nearly half (147/303, 48.5%) of probable NCC cases were a combination of uninsured (18/303, 5.9%), Medicaid funded (74/303, 24.4%), or Medicare funded (55/303, 18.1%) (Table 5).

Discussion

CT brain scan findings were chosen as the initial surveillance tool for the research because of "high sensitivity and specificity for most forms of neurocysticercosis and superiority to MR imaging in identifying calcified granulomas," which are often the only sign of infection in the absence of clinical disease symptoms.(31) According to Del Brutto, "Evidence of lesions highly suggestive of neurocysticercosis on neuroimaging studies" meets major diagnostic criteria for NCC.(33)

Out of the 7,363 CT brain scan reports reviewed, 4.1% of scans described evidence of NCC. Upon analysis of all scans interpreted during the study period by the ten reporting radiologists, it was noted that nine of the ten radiologists reported evidence of NCC on CT brain scan reports. The reporting rate of positive NCC scans read per radiologist ranged from 4.8% to 4.1%, with an average reporting rate of positive scans at 4.3%. The radiologist that did not report any evidence of lesions consistent with NCC on CT brain scans reviewed 248 scans or 3.3% (248/7,363) of total scans conducted during the study period. If the radiologist that did not report any evidence of lesions were to

report NCC lesions at the mean reporting rate of 4.3%, 10 additional NCC cases may have been identified during the study period (Table 6).

The largest single minority group identified were Mexican (68.9%), followed by Central or South American (6.9%); 91.4% identified as Hispanic ethnicity. This is consistent with the literature describing the epidemiological features of confirmed NCC cases. However, two thirds of probable NCC cases were female (66.8%), which differs from studies of confirmed NCC cases. Although differences in infectivity of cysticercosis or natural history of NCC disease based on gender has not been reported,(4) the literature has shown that NCC has a propensity to be more severe in women for reasons poorly understood.(67) It is of epidemiological interest that the religion of two probable NCC cases was identified as Seventh Day Adventist, given that the dietary guidelines for this religion forbid eating pork. It is possible that local transmission of NCC has occurred here as it did in an Orthodox Jewish community in New York City in 1990-1991.(27)

Most of the NCC cases (94.3%; 286/303) presented through the ED, with over half (52.4%) being subsequently admitted to hospital. Total ED visits at the study site totaled 41,379 in 2012, making probable NCC ED encounters account for 0.6% (286/41,379) of the patients seen. The rate of presentation to the ED and hospital admissions at the study site demonstrates the considerable economic implications of this infection. Analysis of payment type for the probable NCC cases in this study demonstrated that public funds (Medicaid, Medicare, uninsured) accounted for the payment of nearly half (48.5%) of patients presenting for treatment.

While many of these NCC cases may represent inactive infection, indicating remote infection manifested only by parenchymal brain calcifications,(9) they were still forwarded to infection control for reporting to Los Angeles County Department of Public Health for follow-up. It has been reported that up to 50% of cases suffer from two or more stages of NCC at the same time, indicating possible repeated exposure and increased potential for spread of the infection to household contacts.(15) A prior study examining NCC cases in Peru has demonstrated that CT brain scan diagnosis exceeds 95% specificity for most forms of NCC infection.(68)

Once a cysticercosis or NCC case is reported to the health department, a public health nurse implements a follow-up investigation that consists of obtaining epidemiological data and collecting a finger-stick specimen to send for serological testing.(69)Enzyme-linked immunotransfer blot (EITB), developed by the Centers for Disease Control and Prevention (CDC), is the most reliable serological antibody-detecting test, with a 98% sensitivity rate for two or more cysts and 100% specificity.(29, 70) In addition to serological testing of each suspected NCC case, EITB testing is also conducted upon the household members to identify tapeworm carriers. Upon identification of a positive serology test, the infected individuals and household contacts are evaluated and offered treatment with antihelminthic therapy and/or steroids if live cysts are identified or otherwise clinically indicated.

Study Limitations

This was a retrospective record review for the year 2012. Because none of the cases had been confirmed with a positive serologic test result or positive biopsy at the time of identification through record review, all cases were considered probable, as defined by Del Brutto and colleagues.(33) Probable NCC cases for the year 2012 discovered during the research record review that took place in 2013 were forwarded to the hospital's infection control department for reporting to LA County Department of Public Health. Serological confirmation data that would allow probable case status to be confirmed was not available at the time of publication.

Generalizability can only be to this hospital population during the 2012 time period designated for research record review. These 303 probable NCC cases are expected to be an underestimate since there are individuals who likely meet the probable NCC case definition who did not present for healthcare due to lack of symptomology, or financial or other barriers to accessing healthcare common in this immigrant population and leading to their being an under-ascertained group.

Conclusions

This study conducted in an East Los Angeles hospital serving primarily immigrant populations from Latin America demonstrates the importance of active case finding for NCC by hospitals. In this study, follow-up of positive CT brain scan findings with medical record review for additional probable diagnostic criteria identified 303 probable NCC cases for the year 2012 that could have been reported to the health

department for subsequent identification and treatment of patient, family, or community members at potential risk. Passive morbidity surveillance for NCC occurs when a person becomes ill and presents to a primary care provider who may order a CT brain scan where a positive finding by the radiologist would possibly trigger a report of the suspected infection to infection control, and the infection control department would then report the infection to the local health department. The local health department then reports the infection to the state health department.(58) With each escalating level, information becomes scarcer and a fraction of cases from the previous level are captured. If any step in this complex process fails to occur, NCC infection is not reported.(24) Identifying barriers to active reporting in hospitals is critical, and strategies need to be implemented to overcome these barriers. While this current research demonstrates the value of active surveillance to improve understanding of the extent of NCC disease burden and underreporting in East Los Angeles, it also points to the need to improve data collection in other areas of the country not currently required to report cysticercosis/NCC infection to their health departments.

Table 2

Diagnostic Criteria for Neurocysticercosis

(Del Brutto OH, et al, Neurology. 2001, with permission from American Academy of Neurology)
Absolute Criteria
Histological demonstration of the parasite from biopsy of a brain or spinal cord lesion
Evidence of cystic lesions showing the scolex or neuroimaging studies
Direct visualization of subretinal parasites by funduscopic examination
Major Criteria
Evidence of lesions highly suggestive of neurocysticercosis on neuroimaging studies
Positive serum immunoblot for the detection of anticysticercal antibodies
Resolution of intracranial cystic lesions after therapy with albendazole or praziquantel
Spontaneous resolution of small single-enhancing lesions
Minor Criteria
Evidence of lesions suggestive of neurocysticercosis on neuroimaging studies
Presence of clinical manifestations suggestive of neurocysticercosis
Positive CSF ELISA for detection of anticysticercal antibodies or cysticercal antigens
Evidence of cysticercosis outside the CNS
Epidemiological Criteria
Individuals coming from or living in an area where cysticercosis is endemic
History of frequent travel to disease-endemic areas
Evidence of a household contact with Taenia solium *infection*
DEGREES OF DIAGNOSTIC CERTAINTY
DEFINITIVE DIAGNOSIS

PRESENCE OF ONE ABSOLUTE CRITERION
PRESENCE OF TWO MAJOR PLUS ONE MINOR OR ONE EPIDEMIOLOGICAL CRITERIA
PROBABLE DIAGNOSIS
PRESENCE OF ONE MAJOR PLUS TWO MINOR CRITERIA
PRESENCE OF ONE MAJOR PLUS ONE MINOR AND ONE EPIDEMIOLOGICAL CRITERIA
PRESENCE OF THREE MINOR PLUS ONE EPIDEMIOLOGICAL CRITERIA

Table 3

Demographics of Probable NCC Patients

Demographics of Probable NCC Patients (N=303)		
Gender	**n**	**%**
Male	100	33%
Female	203	66.9%
Ethnicity		
Hispanic	277	91.4%
African-American	10	3.6%
Caucasian	5	1.6%
Asian	3	0.9%
Other/Unknown	8	2.6%
Age Group (years)		
20-30	11	3.6%
31-40	17	5.6%
41-50	43	14.19%
51-60	42	13.8%
61-70	65	21.4%
71-80	60	19.8%
81-90	52	17.1%
91 and up	11	3.6%
Unknown	2	0.6%
Birthplace		
Mexico	209	68.9%
United States	41	13.5%

Guatemala	11	3.6%
El Salvador	7	2.3%
Korea	2	0.6%
Haiti	1	0.3%
Nicaragua	1	0.3%
Peru	1	0.3%
Ecuador	1	0.3%
Ireland	1	0.3%
Europe	1	0.3%
Unknown	27	8.9%

*Central/South America (Nicaragua, Peru, Guatemala, Peru, Ecuador, &El Salvador) 21/303, 6.9%

Religion	**n**	**%**
Catholic	200	66.0%
Non-denominational	70	23.1%
Christian	10	3.3%
None	8	2.6%
Unknown	6	1.9%
Baptist	2	0.6%
Jehovah's Witness	2	0.6%
Seventh Day Adventist	2	0.6%
Other	2	0.6%
Protestant	1	0.3%

*Unkown, None, Non-denominational, &Other= 86/303, 28.38%

Table 4

2012 Hospital Identified Cases International Classification of Disease (ICD) ICD-9 123.1

ICD-9 123.1 HOSPITAL IDENTIFIED CASES 2012

Location	Age	Ethnicity	CTB Scan performed	Discharge Date	Captured by study
1. Outpatient	30	HISPANIC	No	8/3/2012	No
2. Outpatient	42	HISPANIC	Yes	7/16/2012	Yes
3. Outpatient	77	HISPANIC	Yes	12/26/2012	Yes
4. Inpatient	46	HISPANIC	Yes, but negative	6/12/2012	No
5. Inpatient	29	HISPANIC	Yes	7/9/2012	Yes
6. Inpatient	63	HISPANIC	Yes	8/18/2012	Yes
7. Emergency Dept	40	HISPANIC	No	1/24/2012	No
8. Inpatient	54	HISPANIC	Yes, but negative	2/2/2012	No
9. Inpatient	66	HISPANIC	Yes, but negative	4/30/2012	No
10. Inpatient	47	HISPANIC	Yes	5/2/2012	Yes
11. Emergency	27	HISPANIC	Yes	5/2/2012	Yes
12. Emergency	28	HISPANIC	Yes	5/16/2012	Yes
13. Emergency	65	HISPANIC	Yes	9/5/2012	Yes
14. Emergency	38	HISPANIC	Yes, but negative	9/7/2012	No
15. Inpatient	28	HISPANIC	Yes	9/12/2012	Yes
16. Inpatient	27	HISPANIC	Yes	11/11/2012	Yes
17. Emergency	70	HISPANIC	Yes	11/23/2012	Yes

Table 5

Insurance Payer

INSURANCE PAYER	TOTAL NCC CASES(N=303)	PERCENTAGE (%)
MEDICAID (MEDI-CAL)	74	24.4%
MEDICARE	55	18.1%
UNINSURED	18	5.9%
HMO	118	38.9%
PPO	16	5.2%
WORKER'S COMP	2	0.6%
OTHER PRIVATE	20	6.6%

*Total Public funds (Medi-cal, Medicare,& Uninsured) 147/303, 48.5%

Table 6

Radiologist Reporting Rates

Radiologist (N=303)	***Number of Scans Read**	**% of Scans Positive**	**% of Total** NCC Cases
Radiologist 1	42	4.7%	2(0.6%)
Radiologist 2	301	4.3%	13 (4.2%)
Radiologist 3	41	4.8%	2 (0.6%)
Radiologist 4	283	4.2%	12 (3.9%)
Radiologist 5	2498	4.2%	106 (34.9%)
Radiologist 6	381	4.2%	16 (5.2%)
Radiologist 7	2141	4.2%	91 (30.0%)
Radiologist 8	1143	4.2%	49 (16.1%)
Radiologist 9	285	4.2%	12 (3.9%)
Radiologist 10	248	0 0	0

*Scans read in the year 2012

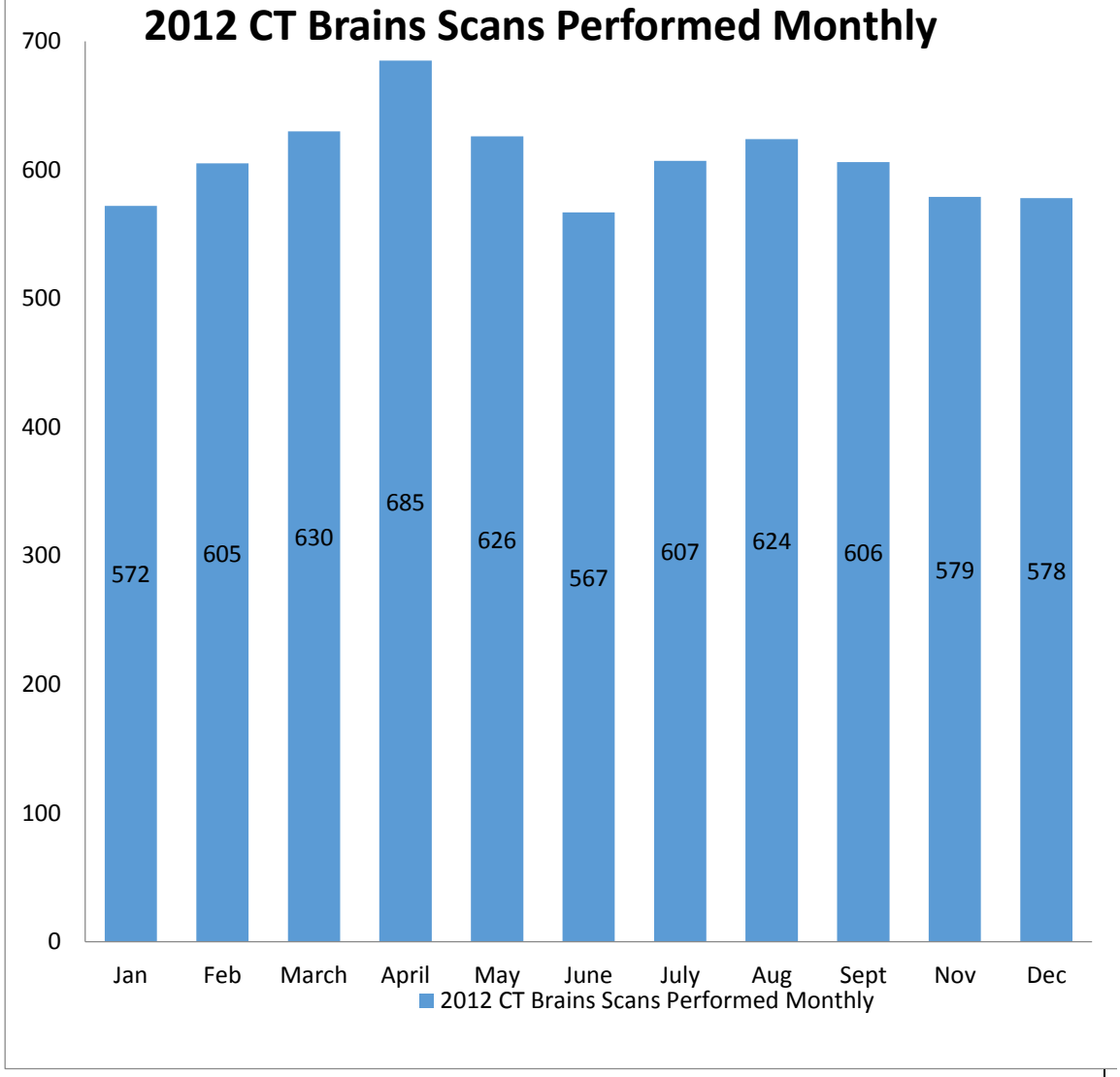

Figure 11.

2012 CT Brain Scans Performed per Month.

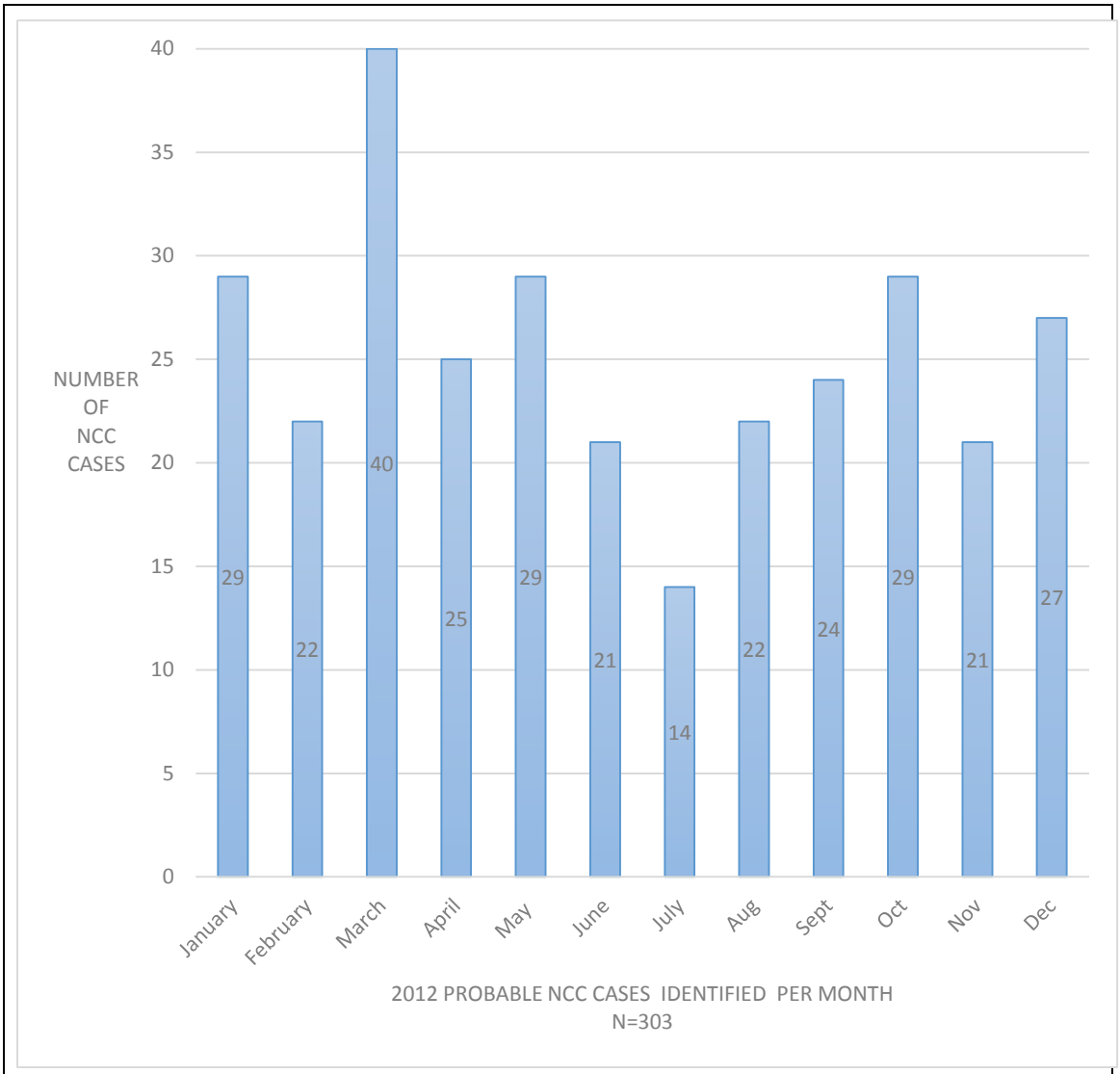

Figure 12.

Probable NCC Cases Identified per Month.

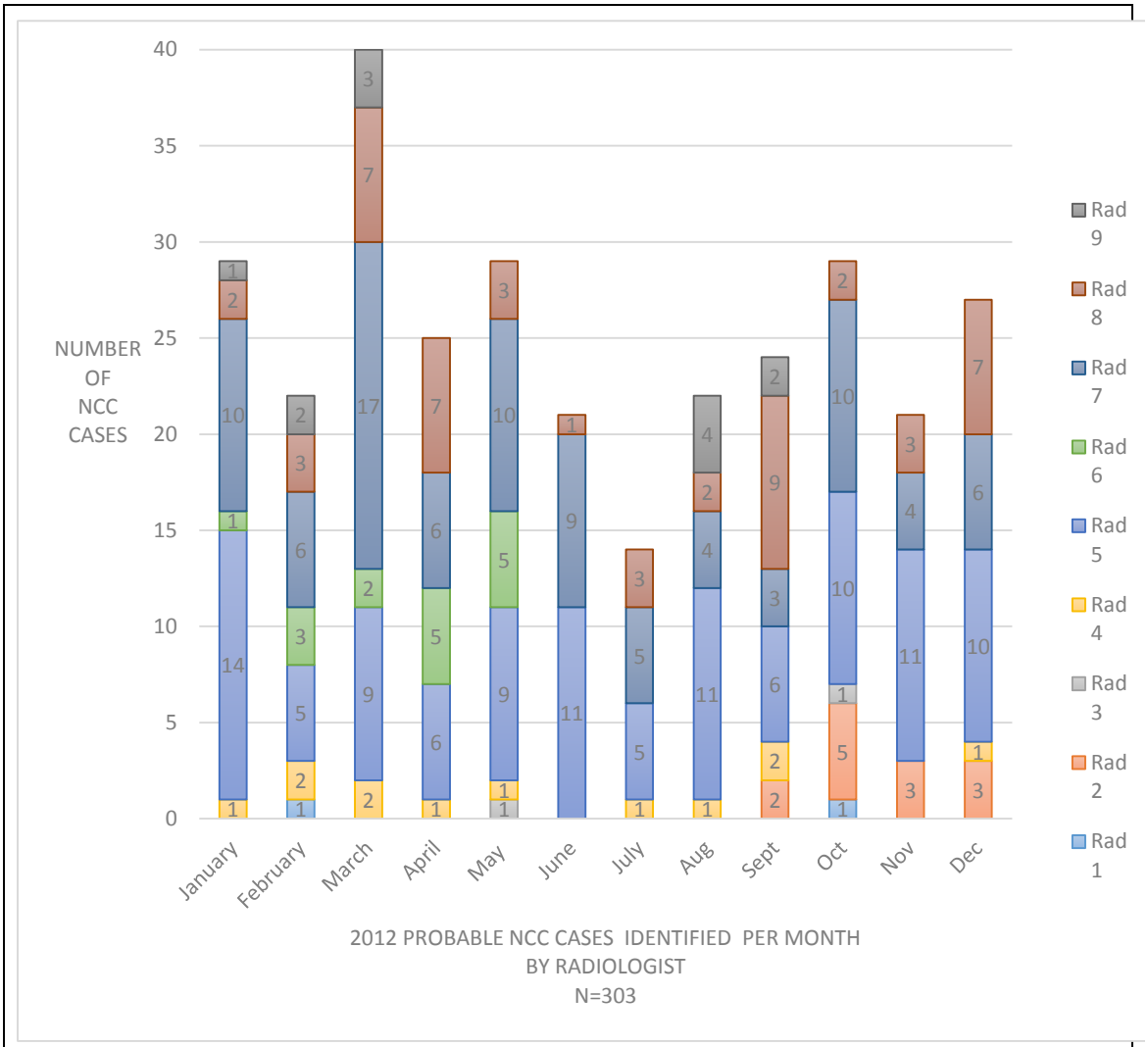

Figure 13.

Probable NCC Cases Reported by Radiologist.

CHAPTER 6: PRESENTING SYMPTOMS AND MORTALITY OF 303 PROBABLE NEUROCYSTICERCOSIS CASES WITH POSTIVE RADIOGRAPHIC IMAGING IN AN EAST LOS ANGELES HOSPTIAL

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Manuscript word count: 2,661 **Tables**: 4 **Figures:**1 **References:**25

Keywords: *Taenia solium*, cysticercosis, seizure, neurocysticercosis, presenting symptoms, headache, mortality

Abstract

Objective: To examine presenting symptoms, mortality data, and location of neurocysticercosis (NCC) lesions and stages in expired probable NCC patients identified in a Los Angeles hospital during 2012.

Design/Methods: A descriptive study was conducted utilizing retrospective review of Computerized Tomography (CT) brain scan reports of 303 probable NCC patients presenting for medical treatment in 2012. Presenting symptoms described in the "INDICATION" section of the CT report were recorded. Mortality rate was calculated.

Results: 21 categories of presenting symptoms were identified during the study.Of the 303 probable cases reviewed, 11/303 (3.6%) presented with seizure. The most common presenting symptom in the study population was headache 75/303 (24.7%).Death occurred in 12 cases (3.9%). All 12 expired cases were staged with parenchymal calcified NCC.

Conclusions: Neurocysticercosispresenting symptoms at this hospital differ from the published literature. At time of death, NCC cases were affected with the inactive form of NCC.

Abstract word limit: 150

Introduction

Cysticercosis is a parasitic infection caused by the larvae of the tapeworm *Taenia solium* (*T. solium*) found in pigs. Most infections occur after eggs from a mature tapeworm are shed in the stool of an infected human and are ingested by pigs, the typical transitional host.(71) After being ingested by the porcine host, the larvae hatch, penetrate the intestines, and migrate through different areas in the body where the cysticercus develop.(63) The transmission cycle is complete when humans, the definitive host, consume the undercooked or raw pork infected with cysticerci. It is also possible for humans to become infected when consuming food other than pork, or water that is tainted with eggs.(39) Symptomatic cysticercosis in humans very often presents as neurocysticercosis (NCC), a severe version of the infection with larvae migrating through the lumen of the intestine and lodging in the brain, eyes, and spinal cord, forming cysts that persist for years causing widely variable clinical presentation.(72) As a result, NCC has been referred to as the"great imitator" for its ability to masquerade as nearly any neurological syndrome.(4) Seizures are typically the most commonly associated presenting symptom of NCC, but it is also known to cause headaches and focal neurological deficits. A recent review article reported that nearly 80% of NCC cases present with seizures.(1, 65) Treatment for NCC is dependent upon several factors, such as location of cysts, stage of infection, severity of symptoms, and host response. The range of treatments include antihelminthic drugs, steroids, analgesics, antiepileptic

medications, ventriculoperitoneal shunting, and surgical removal of cysts (Figure 14). (71)

NCC is the most common parasitic disease of the human central nervous system.(72) NCC infection is endemic in developing countries with poor sanitation and improper slaughterhouse practices and is believed to mainly affect immigrants from Latin America when identified in the United States.(5)However, more recent reports indicate a steady increase in the number of cases acquired in the United States due to contaminated food or water from a human tapeworm carrier.(7, 27) There is no reliable prevalence or incidence for cysticercosis or NCC in the United States due to unreliable reporting systems and the fact that cysticercosis is not reportable in 45 states, with the exception of Texas, Arizona, California, New Mexico, and Oregon.(65)

The purpose of the study was to examine presenting symptoms and mortality data of probable NCC cases in a community hospital in East Los Angeles that serves a primarily immigrant Hispanic population, and then to compare findings to the published literature on other NCC populations. The goal is to provide further understanding of presenting NCC symptoms, and to examine location and classification of NCC infection in those who expired.

Methods

The research was conducted at an urban 373-bed hospital in East Los Angeles that provides care for indigent patients in Los Angeles County. In 2012, the hospital saw 41,379 patients in the Emergency Department (ED), of which 89.8% self-identified as

Hispanic ethnicity. The study site conducted Computed Tomography (CT) brain studies for 7,363 patients. Case finding via retrospective record review of CT brain scan reports in Centris Enterprise Web V3.0 and corresponding medical records in PowerChart was conducted from January 1, 2012 to December 31, 2012. The "INDICATION" of presenting symptoms were recorded exactly as reported by the treating physician and sorted into 21 categories. The 21 categories were based upon the terminology entered into the "INDICATION" portion of the CT brain report by the radiologist.

Computerized Tomography (CT) brain imaging allows for identification of the number and location of NCC lesions, as well as visualization of the four stages of NCC: vesicular, colloidal, granular-nodular, and calcified phases of the parasite in the brain.(36)As a result, CT brain scan was chosen as the screening tool for the retrospective research review due to its high sensitivity and specificity in identifying the various forms of NCC and because it is superior to MR imaging in identifying calcified granulomas, which are often the only sign of NCC infection when clinical symptoms are not present.(31)According to Del Brutto's Diagnostic Criteria for NCC, evidence of lesions highly suggestive of NCC on neuroimaging studies meets major diagnostic criteria for NCC.(33)

Associated patient medical records of triggered probable NCC cases identified on CT brain scan reports were additionally reviewed in PowerChart to verify that minor and epidemiological diagnostic criteria were met for the case definition (Table 7). These variables included presenting symptoms consistent with NCC infection, includingseizure,

headache, stroke symptoms, and places of birth where NCC is endemic, such as Mexico and Latin America.Presenting symptom findings of this study population were then compared to previous publications addressing presenting symptoms and clinical manifestations of NCC patients in various populations. The 21 categories were obtained by reviewing the "INDICATION" on the CT brain scan report and sorted accordingly.

The study received approval by the South Campus General Institutional Review Board at the University of California Los Angeles with a waiver of consent granted for the retrospective record review.

Results

A total of 7,363 CT brain scan reports were reviewed for the year 2012, and 303 probable cases of NCC were identified, giving the hospital a 4.1% prevalence rate for NCC. Death occurred in 3.9% (12/303) of cases. Of these probable cases that expired, age ranged from 46 to 85 years, with mean age 67.1 years; 83.3% (10) of expired cases were female, and 16.6% (2) were male. All 12 expired cases visited the ED and were subsequently admitted to the hospital. Length of stay for the cases who expired ranged from 3 to 75 days, with mean of 20.1 days; 83.3% of expired cases were Hispanic; 8.3% were non-Hispanic; and 8.3% were of unknown ethnicity. Of the study population, 86.5% were born outside of the United States (US), of which 75.8% were born in Mexico and Central or South America, with the largest majority born in Mexico (68.9%). There is currently no reliable prevalence or incidence for cysticercosis or NCC in the US or Mexico for comparison.(73)

While 21 categories of presenting symptoms were identified, just over 75% of identified NCC cases (228/303) presented with one of five types of symptoms (Table 8). The most frequent presenting symptom was headache/migraine, with 24.7% (75/303) of probable cases complaining of this ailment. Seventeen percent (52/303) of patients presented with focal deficits, including CVA/TIA/intracranial hemorrhage, and 14.8% (45/303) of cases were described as having altered level of consciousness (ALOC) on presentation. Nearly 10% percent (30/303) of patients presented with non-fall trauma, and 8.9% (27/303) complained of dizziness/vertigo on admission. Presentation with seizure activity in these hospital cases identified through CT scan record review was identified in 3.6% (11/303) of cases, and history of seizure was found in 10.5% (32/303) of probable cases (Table9).

Physician discharge summary diagnosis information was collected and compared with presenting symptoms to assess for concordance. Two of the 303 (0.6%) probable cases of NCC were given the discharge diagnosis of old cysticercosis and NCC. The five most common physician discharge summary diagnoses, which accounted for 33% (100/303) of probable NCC cases, were headache44/303(14.5%), ischemic cerebral vascular accident 28/303 (9.2%), transient ischemic attack (TIA) 15/303 (4.9%), and seizure 13/303 (4.2%).

Of the probable NCC cases that expired, the length of stay (LOS) ranged from 3-75 days, with a mean of 20.08 days, compared to 4.5 days for the 159 probable NCC cases who were admitted to the hospital but did not die. Of those who expired, 75%

(9/12) of these NCC patients were publicly funded through Medicaid (7/12, 58.3%) and Medicare (2/12, 16.6%), and totaled 240.96 (12 x 20.08) hospital days, compared to 48.5% of publicly funded cases that did not die but were admitted to the hospital. The total hospital days for the admitted NCC cases that did not expire totaled 715.5 (159 x 4.5) days.

All expired cases were reviewed for intraventricular involvement of cysts, subarachnoid cysticercosis, and presence of hydrocephalus, indications that are associated with severe clinical presentation of NCC,(38) but no evidence of these symptoms were found documented on their CT brain scan reports. All expired cases described calcified lesions within the brain parenchyma. With intraparenchymal NCC accounting for up to 70% of all NCC cases and being highly associated with epileptic seizure presentation, we would expect to see that some of these deaths might present with seizure in the ED.(26) Instead, we see that none of the 12 deaths presented with seizure, and the most common presenting symptoms were a combination of cerebral vascular accident (CVA) (2/12; 16.6%), altered level of consciousness (ALOC) (2/12; 16.6%), and weakness (2/12; 16.6%). Three (25%) of the expired 12 probable NCC cases had evidence of prior or acute CVA on their CT brain scan reports, of which 2 were acute and 1 old.(Table 10).

Discussion

A recent review of the literature demonstrated that nearly 80% of symptomatic NCC cases had clinical manifestations of seizure/epilepsy.(1) This is in contrast to the

findings for this study that identified clinical manifestations of seizure in 3.6% (11/303) of cases. The lack of seizure presentation may not imply that the probable NCC cases are overly inclusive, but that the cases likely represent older infections.(4) Identified cases in this study were observed on CT scan to be at the calcified stage of involution, as there was no mention of a scolex, or live tapeworm, in the 303 brain scan reports.By the time an NCC patient begins to present with seizures, the tapeworm is presumed dead and the infection is at least 3 years old.(3) Many of the identified cases in the study seem to represent imported cases with the inactive calcified lesions that have historically not demanded a high priority for follow-up by the public health department. However, these probable NCC cases may suffer from two of more different stages that would indicate repeated exposure, particularly if these cases return to their birth countries periodically.(9, 15) This scenario would indicate that identifying a taeniasis carrier is more likely, and follow-up by public health a higher priority to prevent transmission to household contacts. Further research and follow-up must be conducted to address this possibility. Nearly a quarter of the NCC patients in the present study presented withheadache/migraine (24.7%, 75/303). In contrast, the findings of a recent review publication indicate that 37.9% of NCC patients reported headaches.(1) When examining for symptoms of focal deficits in the present study, the categories of symptoms consistent with CVA/TIA/intracranial hemorrhage were combined and amounted to 17% (52/303) of presenting symptoms. This finding was similar to the review publication that reported 16% of NCC cases presented with focal deficits.(1) Of the cases that expired, 3/12 (25%)

presented with focal symptoms of cerebral vascular accident (CVA) and ataxia (1/12) on admission, slightly higher than the rest of the NCC cases that did not expire. The remaining deceased cases presented with weakness (16.6%), altered level of consciousness (16.6%), fall (8.3%), confusion (8.3%), cardiac arrest (8.3%), headache (8.3%), and altered mental status (AMS) (8.3%) (Table 10).

There was also a difference between physician discharge diagnosis of identified probable cases in the study when compared with presenting symptoms, and only 2 of the identified 303 cases were given a primary discharge diagnosis of cysticercosis or NCC. It is unclear why this discrepancy exists.The treatingphysicians were not queried about how they arrived at the final discharge diagnosis. It is interesting to note that the case number of seizure as a discharge summary diagnosis in probable NCC cases (13/303, 4.2%) was greater than the actual number of cases with presenting symptoms of seizure (11/303, 3.6%). One possible explanation is that the discharge summary of seizure in patients who did not present with the seizure had the seizure after admission, and it was not recorded in the medical record, or the diagnosis was attributed to a patient's history of seizure, which was present in 32/303 (10.5%) cases, and 10 out of the 11 (90.9%) cases presenting with seizure also had a history of seizure disorder identified in their medical record.

The most common discharge diagnosis for probable NCC cases who died while hospitalized was sepsis (5/12, 41.6%), followed by CVA (2/12, 16.6%), acute coronary syndrome (2/12, 16.6%), acute respiratory failure (1/12, 8.3%), transient ischemic attack

(1/12, 8.3%), and unknown cause (1/12, 8.3%). The discharge diagnosis of CVA (2/12, 16.6%) matched with the presenting symptoms for these two patients, while the rest of the cases (10/12, 83.4%) had discharge diagnoses unrelated to their presenting symptoms.

A significant majority of cases 277/303 (91.4%) were classified as Hispanic ethnicity, a finding that is consistent with NCC literature of patients identified in the United States. However, over two-thirds of presenting cases were female (203/303, 66.8%), which was not consistent with NCC literature. Published evidence does not suggest gender predilection in NCC.(4) One possible explanation for findings in the present study is that females tend to access healthcare services more than men, as indicated by increased hospital presentation.(74)

While there was no evidence of hydrocephalus, periventricular, or subarachnoid involvement in the twelve expired cases, six of them did demonstrate evidence of periventricular ischemic changes of the white matter on CT brain scan reports. Periventricular white mater changes are often associated with risk factors such as hypertension, reduced cerebral bloodflow, diabetes mellitus, coronary artery disease, and atherosclerosis.(75) When these expired cases' medical histories were reviewed for these risk factors, evidence of hypertension in their medical history was present in 83.3% (10/12) of their records. Just under half (41.6%; 5/12) of the expired cases had evidence of coronary artery disease in their records, and 66.6% (8/12) of expired cases were diabetic.

A published report in 2007 by Sorvillo and colleagues summarized deaths from cysticercosis in the United States and found Latino/Hispanic men to have a higher adjusted rate ratio for mortality relative to white men, and death in the Latino/Hispanic male population occurs at a mean age range of 40.5 years.(76) Where the current study findings differ from the literatureis that most of the 12 deaths in the present study were female (83.3%), and the age at death was higher (mean age 67.1 years) compared to the primarily male deaths at an average age of 40.5 years, as reported by Sorvillo. The mean age for probable NCC cases identified in the present study who did not expire was 64.7 years.

Limitations

Limitations of the study included inability to confirm NCC infection through brain biopsy or*T. solium* antibody-specific serological testing, EITB(enzyme-linked immunoelectrotransfer blot assay) or ELISA (enzyme-linked immunoassay). Therefore, all identified cases were probable.(69) The clinical manifestations of NCC are varied and nonspecific, and it is not unusual for patients to experience a range of symptoms over time. However, the study design of reviewing the CT brain"INDICATION" did not allow for multiple symptoms to be recorded and might obscure the true clinical presentation of the disease. The medical records were not set up to distinguish between race and ethnicity, and any differences among these groups were not measurable. Selection bias is another limitation, as the study only included patients who presented for healthcare treatment. Noncontrast CT brain scan was used as the primary screening tool to identify

probable NCC cases and may have missed NCC cases with small enhancing lesions without edema that would be better detected with contrast CT brain scan.

Conclusion

There are many gaps identified in the literature regarding the understanding of the epidemiology of cysticercosis and NCC in United States, most profoundly, the burden of disease. More research on cysticercosis and NCC is indicated in order to further examine transmission dynamics to develop prevention initiatives for persons at risk for this disease. Increasing health care providers' awareness of cysticercosis and NCC symptoms may lead to improved detection, reporting, and treatment of persons infected with this parasite. A follow-up study with confirmatory testing and examination of differences in NCC patients with and without seizure would be beneficial.

Table 7

Diagnostic Criteria for Neurocysticercosis

(Del Brutto OH, et al, Neurology. 2001, American Academy of Neurology)
Absolute Criteria
Histological demonstration of the parasite from biopsy of a brain or spinal cord lesion
Evidence of cystic lesions showing the scolex or neuroimaging studies
Direct visualization of subretinal parasites by funduscopic examination
Major Criteria
Evidence of lesions highly suggestive of neurocysticercosis on neuroimaging studies
Positive serum immunoblot for the detection of anticysticercal antibodies
Resolution of intracranial cystic lesions after therapy with albendazole or praziquantel
Spontaneous resolution of small single-enhancing lesions
Minor Criteria
Evidence of lesions suggestive of neurocysticercosis on neuroimaging studies
Presence of clinical manifestations suggestive of neurocysticercosis
Positive CSF ELISA for detection of anticysticercal antibodies or cysticercal antigens
Evidence of cysticercosis outside the CNS
Epidemiological Criteria
Individuals coming from or living in an area where cysticercosis is endemic
History of frequent travel to disease-endemic areas
Evidence of a household contact with Taeniasolium *infection*
DEGREES OF DIAGNOSTIC CERTAINTY

DEFINITIVE DIAGNOSIS
PRESENCE OF ONE ABSOLUTE CRITERION
PRESENCE OF TWO MAJOR PLUS ONE MINOR OR ONE EPIDEMIOLOGICAL CRITERIA
PROBABLE DIAGNOSIS
PRESENCE OF ONE MAJOR PLUS TWO MINOR CRITERIA
PRESENCE OF ONE MAJOR PLUS ONE MINOR AND ONE EPIDEMIOLOGICAL CRITERIA
PRESENCE OF THREE MINOR PLUS ONE EPIDEMIOLOGICAL CRITERIA

Table 8

Presenting Symptoms of Probable Neurocysticercosis Cases

Symptoms	**N = 303**	**%**
Headache	75	24%
ALOC	45	14%
Dizziness/Vertigo	27	9%
Weakness	17	5%
Trauma	30	10%
Syncope	7	2%
Stroke/TIA/Bleed	52	17%
Confusion	8	2%
Seizures	11	3.6%
AMS	3	1%
Falls	8	2%
Ataxia	3	1%
Pain	4	1%
Mass	3	1%
VP Shunt	2	0.6%
Eye Redness	2	0.6%
Memory Loss	2	0.6%
Cardiac Arrest	1	0.3%
Meningitis	1	0.3%
Hearing Loss	1	0.3%
Vomiting	1	0.3%

Table 9

Demographics of Probable Neurocysticercosis Patients

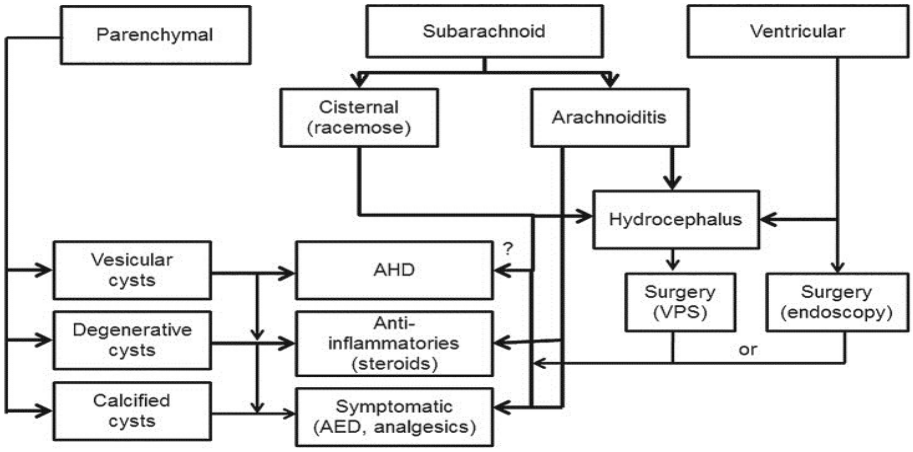
Demographics of Probable NCC Patients (N=303)		
Gender		
Male	100	33%
Female	203	66.9%
Ethnicity	**n=303**	**%**
Hispanic	277	91.4%
African-American	11	3.6%
Caucasian	5	1.6%
Asian	3	0.9%
Other/Unknown	8	2.6%
Birthplace	**n=303**	**%**
Mexico	209	68.9%
United States	41	13.5%
Guatemala	11	3.6%
El Salvador	7	2.3%
Korea	2	0.6%
Haiti	1	0.3%
Nicaragua	1	0.3%
Peru	1	0.3%
Ecuador	1	0.3%
Ireland	1	0.3%
Europe	1	0.3%
Unknown	27	8.9%

*Central/South America (Nicaragua, Peru, Guatemala, Peru, Ecuador, & El Salvador) 21/303, 6.9%

Table 10
Mortality

N=303	**%**	
Total Deaths	12/303	3.9%
Male	2/12	16.6%
Female	10	83.3%
Birthplace		
Mexico	9	75%
US	1	8.3%
Guatemala	1	8.3%
Unknown	1	8.3%
Visited ED on admission	12	100%
Admitted to Hospital	12	100%
Presenting Symptoms		
(ALOC)	2	16.6%
Weakness	2	16.6%
Cerebral Vascular Accident	2	16.6%
Fall	1	8.3%
Headache	1	8.3%
Altered Mental Status (AMS)	1	8.3%
Ataxia	1	8.3%
Confusion	1	8.3%
Cardiac Arrest	1	8.3%
Final Diagnosis		
Sepsis	5	41.6%

Acute Coronary Syndrome	2	16.6%
CVA (Ischemic)	2	16.6%
Acute respiratory failure	1	8.3%
(TIA)	1	8.3%
Unknown	1	8.3%
Ethnicity		
Hispanic	10	83.3%
Caucasian	1	8.3%
Unknown	1	8.3%
Insurance Payer		
Medical/Medicaid	7	58.3%
Medicare	2	16.6%
HMO	2	16.6%
Private	1	8.3%
Intraventricular involvement	**0**	**0%**
Subarachnoid involvement	**0**	**0%**
Hydrocephalus involvement	**0**	**0%**
Parenchymal involvement	**12**	**100%**
Vesicular stage	**0**	**0%**
Colloidal stage	**0**	**0%**
Nodular stage	**0**	**0%**
Calcified stage	**12**	**100**



Neurol Clin Pract. Apr 2013; 3(2): 118–125.doi: 10.1212/CPJ.0b013e31828d9f17

Figure 14.

Neurocysticercosis Treatment Algorithm.

CHAPTER 7: PRESENCE OF PROBABLE NEUROCYSTICERCOSIS INFECTION IS ASSOCIATED WITH ACUTE STROKE IN A LOS ANGELES COMMUNITY HOSPITAL

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Manuscript word count: 2,934 **Tables:** 4 **Figures:** 5 **References:** 19

Keywords: *Taenia solium*, risk factors, neurocysticercosis, ischemic stroke, intracranial hemorrhage, transient ischemic attack

Abstract

Background and Purpose: Presence of neurocysticercosis (NCC) is a known, yet under-appreciated risk factor for cerebrovascular accident (CVA). CVA has been reported in 3%-12% of NCC cases. The purpose of this study was to determine if probable NCC infection is an independent risk factor for acute CVA in patients treated at a Los Angeles community hospital in 2012.

Methods: Probable NCC cases from a previous report were included in the study population identified through retrospective medical record review in a community hospital and compared to CVA and Transient Ischemic Attack (TIA) cases in the analysis. Established clinical risk factors for CVA were controlled for.

Results: A total of 850 patients were included in the final analysis. Of the probable NCC cases, 86 (28.3%) cases demonstrated evidence of previous CVA on noncontrast Computerized Tomography (CT)brain scan report; 40 (13.2%) cases demonstrated evidence of acute CVA; and 21(6.9%) cases demonstrated evidence of both acute and previous CVA. Probable NCC infection was an independent risk factor ($p<.001$) for acute CVA after controlling for associated clinical risk factors. The odds of acute stroke for probable NCC-infected persons were nearly 25 times that of noninfected persons in this study.

Conclusions: The presence of prior stroke in the probable NCC study population (28.3%) was more than double that described in the literature (12%).(15)NCC infection is an independent risk factor for acute stroke in this study population.

Key words: acute ischemic stroke, neurocysticercosis, hemorrhagic stroke, risk factor

Abstract word limit: 250

Introduction

Cysticercosis is a zoonotic infection caused by the larval pork tapeworm, *Taenia solium*, infecting humans in developing countries, mostly Latin America.(33) The

neurological form of the disease, known as neurocysticercosis (NCC), is the most serious and occurs when the larvae migrate from the gastrointestinal tract to the central nervous system such as the brain, spinal cord, and eyes.(65) This infection is the result of a two-host lifecycle involving pigs and humans, where pigs serve as the intermediary host and humans as the definitive host. NCC and is a major public health challenge in the developing world, particularly in Latin America. Reports of local transmission in non-endemic countries have increased due to the growing number of immigrants and can occur through fecal-oral transmission through ingestion of eggs excreted in the fecal matter of a human tapeworm carrier infected with taeniasis.(7)

Neurocysticercosis is most often associated with acquired seizure disorder, an association that has overshadowed examination of NCC infection as a risk factor for stroke, due to the assumption that NCC manifests primarily as a seizure disorder. NCC infection has demonstrated itself to cause significant disability and possibly death in patients despite their lack of other cerebrovascular risk factors.(13) A recent review article reports that stroke syndromes are identified in about 3% of NCC patients.(39) Sotelo and colleagues reported an 11.8% incidence of ischemic stroke in NCC patients.(15) Incidence reporting for hemorrhagic stroke in NCC patients could not be found in the literature, demonstrating the importance of investigating NCC infection as a risk factor for stroke, another highly disabling neurological disorder and the current fourth leading cause of death in the United States.(77)

Subjects and Setting

This study was approved by the South Campus General Institutional Review Board at University of California Los Angeles with a Study Site Authorization Agreement. A waiver of consent was granted due to no human subject interaction with researchers. Trained and certified abstractors reviewed clinical data and obtained demographic and clinical information from the medical chart.

Methods

A retrospective medical record review of all acute stroke and transient ischemic attack (TIA) patients treated in 2012 at a primary stroke center in Los Angeles was conducted by review of 7,363 CT brain scan reports and associated patient medical records from January 1, 2012 to December 31, 2012. The primary aims of the study were to determine if probable NCC infection is an independent risk factor for previous or acute CVA in patients treated at a Los Angeles community hospital. Other aims included comparing mortality rates and length of stay (LOS) in stroke, TIA, and probable NCC cases. The details of this study are based upon a previous report that retrospectively identified 303 probable NCC cases in the same urban Los Angeles hospital.(77) All NCC cases in the previous report met probable diagnostic criteria based upon Del Brutto's Diagnostic Criteria for Neurocysticercosis.(33) Stroke program patient lists were matched against International Classification of Disease, 9th Edition (ICD-9) codes for 434.91, 431, 430, 435, 435.8, and 435.9 identified on discharge for 2012. Stroke and TIA patients who appeared on both lists were included in the study and comprised 547 cases. In

addition, all stroke and TIA patients included in the study were treated by a board certified neurologist and met clinical and or diagnostic criteria for stroke or TIA, based on current clinical practice guidelines.(42) Finally, stroke and TIA patients in the study were compared against the probable NCC cases and reviewed for duplicates. Overlapping cases remained in the probable NCC population and were removed from the stroke and TIA list. Patient data were de-identified.

Statistical Analysis

Statistical analysis was performed using SAS statistical package Version 9.2 (SAS Institute, Inc, Cary, NC), andp-value <0.001 was considered statistically significant. Patients were classified categorically (YES, NO) according to presence or absence of previous stroke and acute stroke on CT brain scan during their hospital visit. Descriptive statistics were computed for demographic and clinical characteristics, using means and standard deviations for continuous measures or frequencies, and percentages for categorical variables. Since acute stroke and previous stroke were the categorical outcome variables, logistic regression was used to examine whether NCC was associated with either of these two outcomes aftercontrolling for nine clinical factors.These nine clinical factor variables were chosen on the basis of being associated with both NCC and stroke.(42, 48)These nine clinical factors in the model consisted of (1) hypertension, (2) hyperlipidemia, (3) history of seizure, (4) history of coronary artery disease (CAD), (5) atrial fibrillation, (6) diabetes mellitus, (7) smoking, (8) history of depression, and (9) carotid stenosis (Table 13). The logistic regression model was fully adjusted for

demographics (age, sex, ethnicity) and all clinically associated factors described above. Length of hospital stay (LOS) was recorded as a count variable, and data were analyzed using a Poisson regression to model the outcome of clinical risk factors on LOS.

Results

A total of 7,363 CT brain scan reports were reviewed. The total sample size included 850 patients, of which 547 were treated for acute ischemic stroke, hemorrhagic stroke, and transient ischemic attack (TIA). The probable NCC cases comprised 303 patients, with all cases described by the radiologists as calcified lesions. Ischemic strokes treated with non-tissue plasminogen activator (tPA) comprised 240 (43.8%) patients in the sample, ischemic strokes treated with tPA totaled 62 (11.3%), intracranial hemorrhage (ICH) patients totaled 133 (24.3%), and TIAs totaled 112 (20.4%). Out of the 7,363 CT brain scans reviewed during the study period, 126 patients (1.7%) had evidence of NCC and stroke, both acute and prior, on the radiologists' reports. Of the 303 probable NCC cases, 86 (28.3%) cases demonstrated evidence of previous CVA on CT scan report, 40 (13.2%) cases demonstrated evidence of acute CVA,and 21(6.9%) cases demonstrated evidence of both acute and previous CVA. Of the probable NCC cases presenting with evidence of acute stroke, 29 (72.5%) were ischemic, 10 (25%) were hemorrhagic, and 1 had both ischemic and hemorrhagic stroke (2.5%). For probable NCC cases presenting with evidence of previous stroke, 83 (96.5%) presented with previous ischemic CVA and 3 (3.4%) presented with prior hemorrhagic stroke and prior aneurysm (Figures15and 16; Table 12).

Mean age of the probable NCC acute CVA patients was 62 years old, with a range of 46-96 years old. Eighty-five percent of cases (34/40) were recorded as Hispanic, 5% (2/40) were African American, 5% other, 2.5% (1/40) Caucasian, and 2.5% (1/40) Asian. Sixty-five percent (26/40) were female and the remaining 35% (14/40) were male. The majority of cases were born in Mexico (67.4%) (Table 12).

Clinical risk factors were compared in probable NCC patients with acute and previous stroke. Of probable NCC patients, 83% with acute stroke demonstrated evidence of hypertension in their medical record compared to 71% with prior stroke. Forty-five percent of probable NCC patients with acute stroke also had diabetes, slightly higher than the 38% diabetes rate in probable NCC patients with prior stroke. Rates for coronary artery disease (CAD) were equal at 40% in both probable NCC acute and prior stroke groups. Hyperlipidemia (HLD) was higher in the probable NCC acute stroke group (35%) versus the probable NCC prior stroke group (22%). Smoking rates were equal, at 15% for both groups. Atrial fibrillation (A-fib) rates were nearly equal, with 15% showing a history of A-fib in the acute stroke group and 14% with a history of A-fib in the prior stroke group. Seizures were also similarly equal in both probable NCC groups, with 13% of acute strokes having a history of seizure versus 12% of prior strokes having a history of seizure. Depression was comparable in both groups, with 13% of the acute stroke group being affected versus 14% in the prior stroke group. Carotid stenosis (CS) did not notably affect either group; 2% of probable NCC acute strokes were affected by CS versus 1% in probable NCC prior stroke cases (Table 13).

Location and type of previous and acute infarcts in probable NCC patients ranged widely, with the most common types of ischemic infarcts being prior stroke (25.5%, 22/86), followed by acute strokes located in the basal ganglia (22.5%, 9/40). In prior stroke patients with probable NCC, 72.7% (16/22) of the basal ganglia infarcts were described as lacunar. Lacunar infarcts are small, noncortical infarcts that result from a blockage of a small branching cerebral artery. They are usually associated with silent stroke, and patients with this types of stroke are often unaware that they had a stroke due to the lack of typical stroke symptoms that would cause a person to seek medical attention (Table 14).(78)

Probable NCC infection was not statistically significant as a risk factor for prior CVA. Presence of carotid stenosis [Odds Ratio (OR) 1.42; 95% confidence interval (CI), 0.73-2.74], Hispanic ethnicity (OR 1.67; 95% CI, 0.94-2.95), African-American ethnicity (OR 1.33; 95% CI 0.65- 2.69), and Non-Hispanic Caucasians (OR 2.25; 95% CI 0.85-5.98) were associated with OR >1.0 for prior stroke but were not statistically significant. Male sex and age were significant for prior CVA ($p<.001$) but had an OR <1.0.

Probable NCC infection was significant as an independent risk factor ($p<.001$) for acute CVA, after controlling for associated clinical risk factors. The OR of acute stroke for probable NCC-infected persons was calculated to be nearly 25 times (24.59) that of non-infected persons in this study (95% CI, 15.2-39.7). History of seizure disorder was also significant as an independent risk factor ($p<.001$) (OR 2.94; 95% CI 1.53-5.64) for acute stroke with an OR of 2.94 times that of a person without seizure.

African-American ethnicity (OR, 1.38; 95% CI 0.6-3.19), history of coronary artery disease (OR 1.31; 95% CI 0.82-2.10), smoking (OR 1.5; 95% CI 0.97-2.42), depression (OR 1.71; 95% CI 1.04-2.83), history of seizure disorder (OR 2.94; 95% CI 1.53-5.64), and hyperlipidemia (OR 1.39; 95% CI 0.91-2.14) were associated with Odds Ratio> 1.0 for acute stroke but were not statistically significant (Table 11).

Presence of two clinical risk factors, hypertension and diabetes mellitus, were associated with increased LOS ($p<.001$), while carotid stenosis, atrial fibrillation, hyperlipidemia, history of seizure, and history of coronary artery disease were not. Smoking and depression were associated with decreased ($p<.001$) LOS. Receiving rt-PA was significant ($p<.001$) for a higher number of days in the hospital, with a mean stay of 9.03 days versus non-tPA ischemic strokes with a mean stay of 3.12 days (Tables 13 and14). Probable NCC infection as a risk factor was significant for a shorter LOS ($p<.001$) in the study. The mean LOS for probable NCC cases was 4.5 days. The TIA patients had a LOS that was 3.7 days, and no deaths reported during the study period (Figure 17; Table 12).

The mortality rate for probable NCC cases was 3.9% (12/303), and 3/12 (25%) of the expired NCC cases had evidence of old and acute stroke on CT brain scan report (2 with acute CVA and 1 with prior CVA). In comparison, ICH patients had the highest mortality rate, with 16.5% (22/133) of patients dying, and the longest LOS at 15.4 days (Figures 17 and 20).

Discussion

Evidence of previous stroke in the probable NCC study population (28.3%; 86/303) was more than double the high estimate identified in a previous study (12%). However, NCC infection was not a statistically significant risk factor for prior stroke.(15) For acute stroke, 13.2% (40/303) of probable NCC cases demonstrated evidence on CT scan, slightly higher than the same estimate of 12% in a previous study.(15)The current study demonstrates that probable NCC infection is a strong and independent risk factor ($p<.0\ 01$) for acute stroke in this study population, even after adjustment for nine clinically associated stroke risk factors: hypertension, hyperlipidemia, history of seizure, history of coronary artery disease, atrial fibrillation, diabetes mellitus, smoking, history of depression, and carotid stenosis, as well as age, sex, and ethnicity.(42, 48) This study supports a previous finding that showed NCC to be an independent risk factor for stroke.(60) After controlling for demographic and clinical factors, the OR of acute stroke for probable NCC-infected persons were nearly 25 times (24.59) that of non-infected persons in this study (95% CI, 15.2-39.7). It was hypothesized that presence of multiple clinical risk factors would be associated with increased LOS. However, NCC, smoking, and depression were actually associated with decreased LOS.

The 303 probable NCC cases identified were parenchymal calcified lesions and presumed to be the inactive form of the infection. This inactive form of NCC has not been historically associated with stroke in prior studies. It is possible that there are multiple NCC cases suffering from more than one stage of NCC if they have ongoing

exposures to the agent, *T. solium*. However, such information was not included in the study subjects' CT brain scan reports. It is also important to note that contrast-enhanced CT brain scans may detect this type of multiple stage NCC scenario more sensitively than CT brain scan without contrast, but study subjects only underwent CT brain without contrast.(79)

The subarachnoid cystic form of NCC, the type of lesion most commonly associated with stroke, was not found to be present in this study population because NCC lesions were not specified to be in the subarachnoid spaces on CT brain scan reports.(21) A previous study has described the mechanism of lacunar stroke occurring in seven NCC cases due to endarteritis as a result of occlusion in a terminal vessel with a nearby cysticerci in the suprasellar cistern, thereby, relating the occurrence of vascular and tissue inflammation, causing stroke to the proximity of the parasite.(21, 80) It was not possible in this study to precisely examine this relationship of proximity of cysticercosis lesions to proximity of stroke location, due to the lack of location specification for cysticercosis lesions on CT brains scan reports.

While the probable NCC-infected cases had a mean LOS of 4.5 days, longer than the non-tPA ischemic stroke cases (3.1 days), NCC infection was determined to be associated with shorter LOS ($p<.001$), likely due to the fact that 132 of the 303 cases (43.5%) were admitted to the hospital for 1 day or less. The patients receiving tPA had a LOS almost 3 times that of the non-tPA cases (9.03 days versus 3.1 days, respectively), yet receiving tPA was not associated with an increased mortality rate (3.2% versus 5.4%)

despite the slightly increased risk of bleeding inherent in thrombolytic treatment for acute ischemic stroke.(43) It was of interest that the TIA cases had a longer average LOS than the non-tPA ischemic stroke cases (3.7 days versus 3.1 days), since TIA cases are generally thought of as less seriously ill than acute stroke cases.(44) It is also of interest that the mortality rate for TIA was 0% while the non-tPA ischemic stroke mortality rate was 5.4%, higher than even the tPA ischemic stroke group of 3.2%. The LOS and mortality rate for ICH cases was expected to be highest of all the groups due to the associated mortality rate of this type of stroke in the literature.(47) The study data supported this hypothesis; both LOS and mortality rates for ICH cases were the highest of all groups, with an average LOS of 15.4 days and a 16.5% mortality rate (Figures 17 and20).

The number of stroke and TIA admissions averaged 45.58 cases per month and was generally consistent with a range of 42-60 cases per month (Figure 18). Admission rates of probable NCC cases demonstrated more variance, with a range of 14-40 cases per month and an average of 25.25 cases per month (Figure 19).

Limitations

This study has several limitations. First, this is an observational study of patients who were admitted to a community hospital in Los Angeles in 2012. Data may not be generalizable to a broader population. The identified NCC cases were probable due to unavailability of confirmatory testing. Another risk factor clinically associated with stroke outcomes is obesity. However, it was not possible to abstract such data from the

medical record due to presence of weight recordings without height. Ischemic strokes were not differentiated into thrombotic, embolic, and hemorrhagic strokes, and were not classified as parenchymal or subarachnoid. The precise location of the lesions in the probable NCC cases were often not specifically identified in the radiology reports, making it difficult to assess the proximity between the lesion and any reported stroke evidence on the same report. There are other clinical risk factors for stroke, such as sickle cell anemia and perforated foramen ovale, to name a few, that were not controlled for due to the effect of decreasing power in the data analysis while also increasing covariate factors to adjust for.(45)

Conclusions

This study has demonstrated that presence of probable NCC is independently associated with acute stroke in this population when other clinical risk factors are controlled for. NCC infection is known to be a disabling infection due to the association with acquired seizure disorder leading to disability and even death. By increasing awareness, education, and prevention efforts to this target population, health professionals may be able to help patients prevent future infection and reduce the incidence and disability for stroke and NCC through targeted education outreach. More research is indicated to further study the mechanisms and pathophysiological associations of NCC infection on stroke.

Acknowledgments

We acknowledge the assistance of Jennifer Bradbury, RN, BSN, PHN; Carolyn Daley, BS; Casandra Amara, RN, BSN, PHN in patient data collection, and White Memorial Medical Center for their support of this study.

Disclosures

The authors report no conflicts of interest.

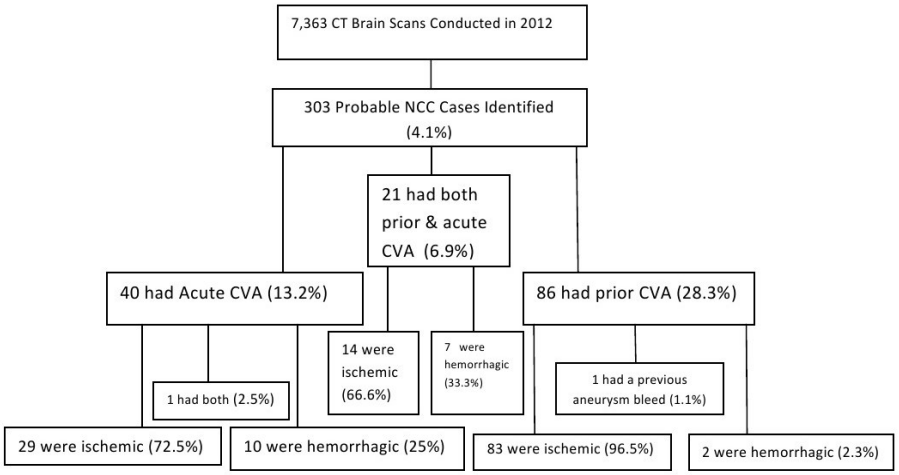


Figure 15.

Breakdown of Acute and Prior CVAs in Probable NCC Cases.

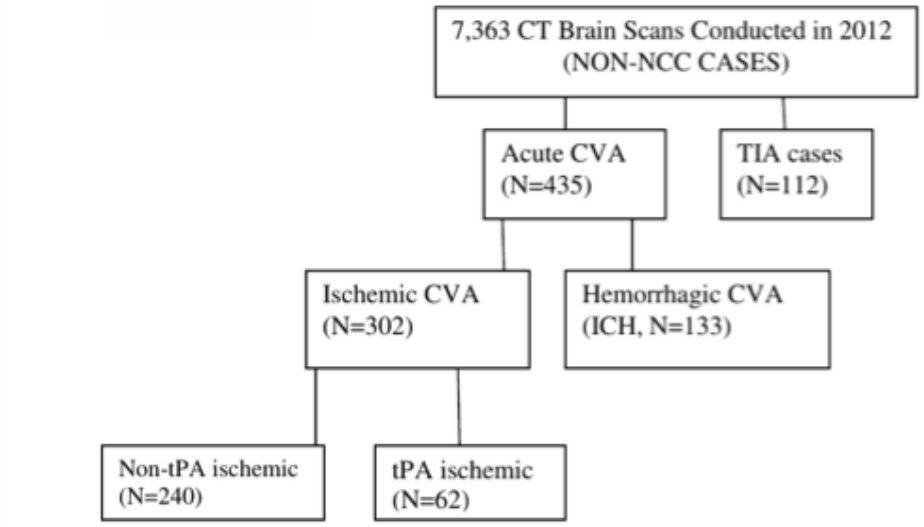


Figure 16.

Breakdown of Acute and Prior CVAs in Non-NCC Cases.

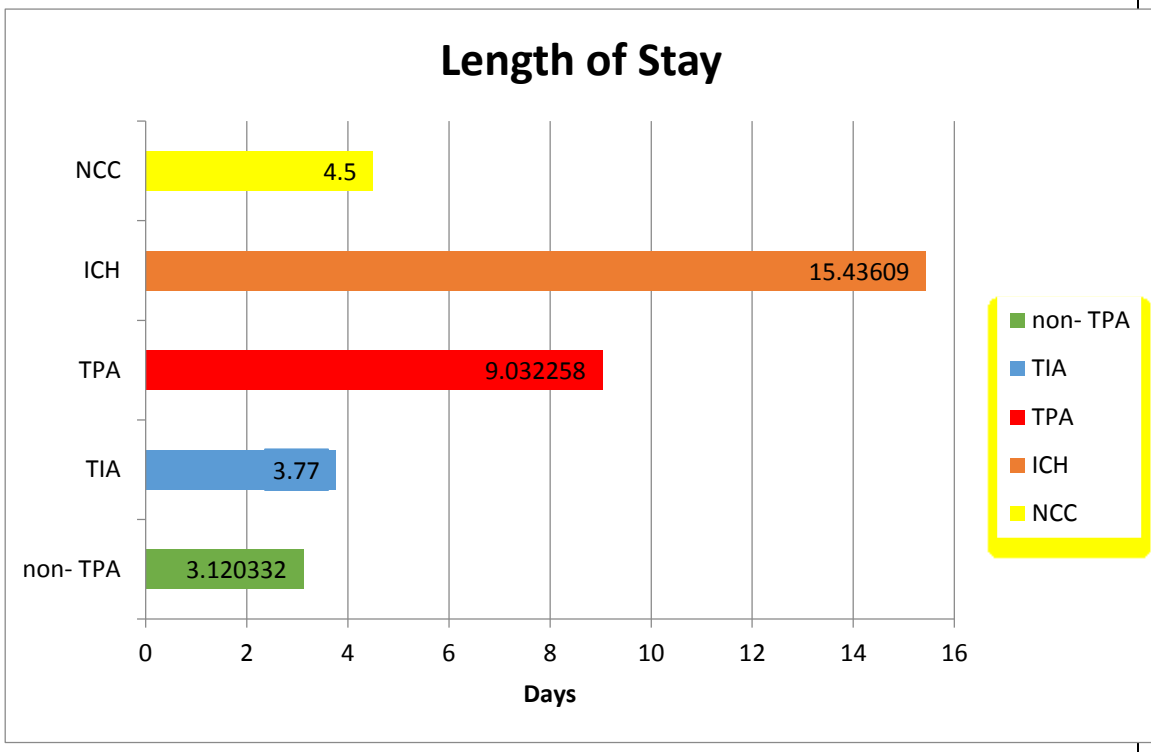
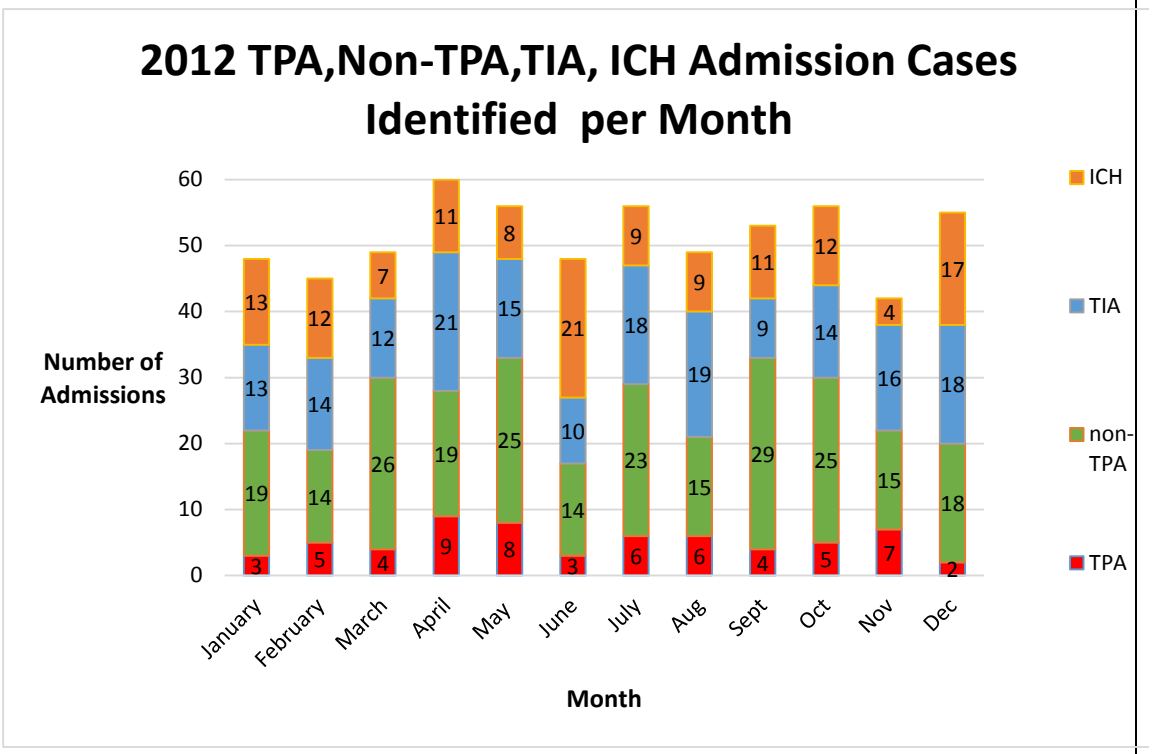


Figure 17.

Hospital Length of Stay.



ICH: Intra-cranial hemorrhage; TIA:Transient ischemic attack; non-TPA=not treated with TPA; TPA=tissue plasminogen activator

Figure 18.

Number of Admissions per Stroke Category.

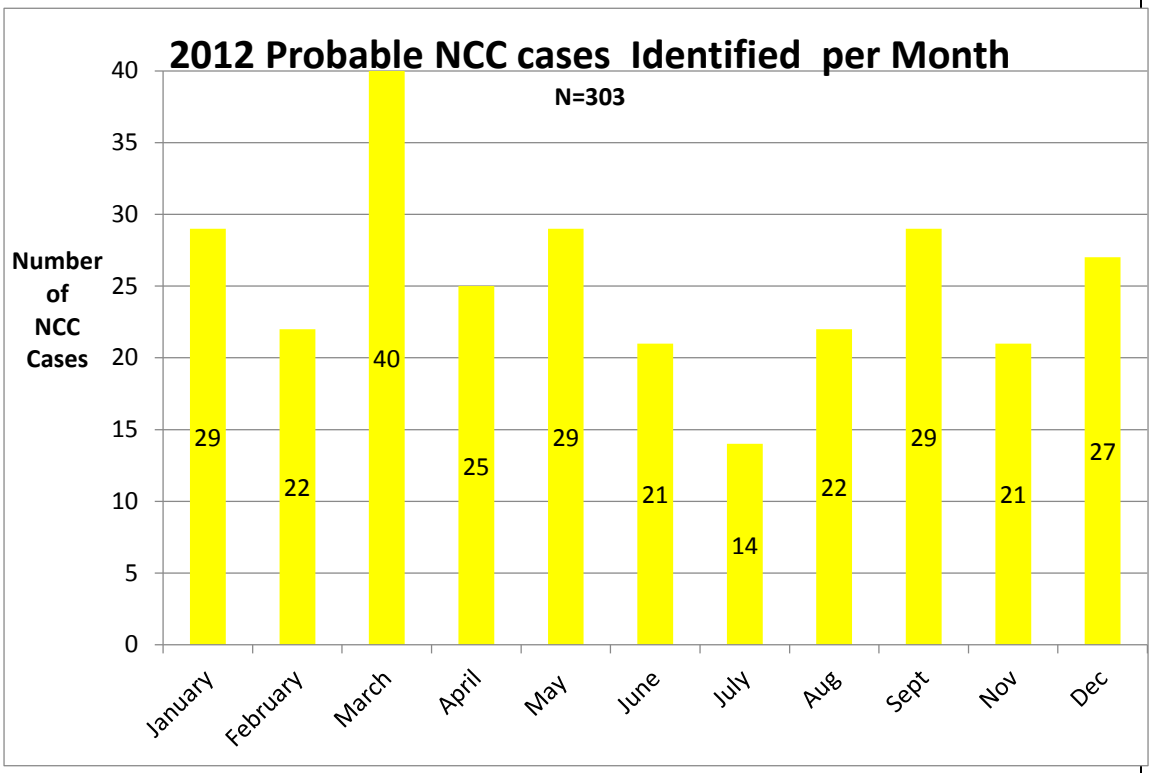


Figure 19.

Probable NCC Cases Identified per Month.

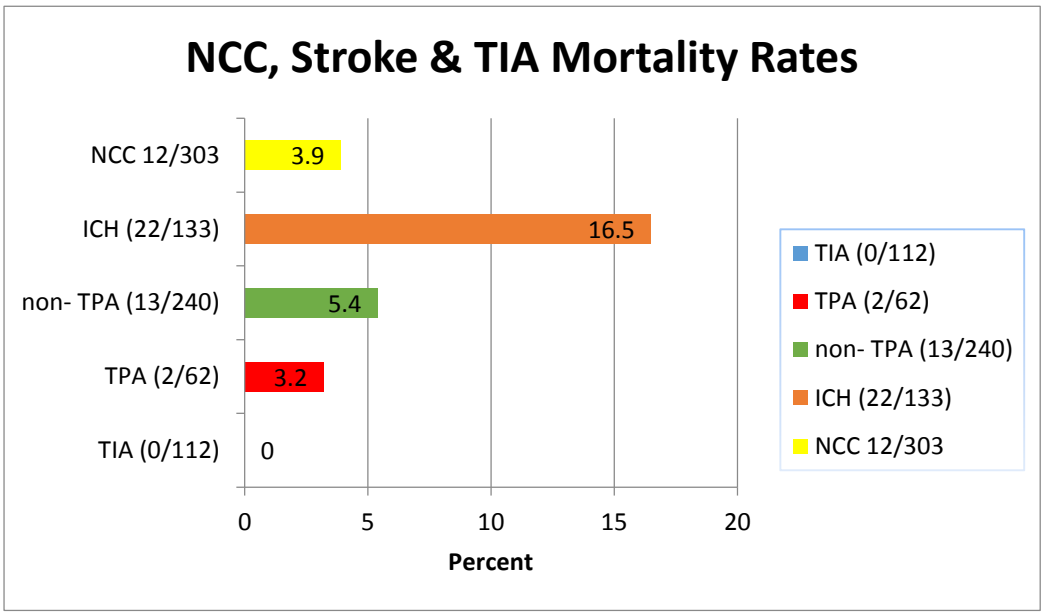


Figure 20.

NCC, Stroke, and TIA Mortality Rates.

Table 11

Logistic Regression Model for Probable NCC as a Risk Factor for Acute CVA

Analysis of Maximum Likelihood Estimates						
Parameter		**DF**	**Estimate**	**Standard Error**	**Wald Chi-Square**	**Pr > ChiSq**
Intercept		1	1.4610	0.5647	6.6931	0.0097
NCC	**1**	1	1.6012	0.1225	170.7960	<.0001
AGE		1	-0.00655	0.00657	0.9938	0.31
Ethnicity						
Hispanic	**1**	1	0.1399	0.1909	0.5371	0.46
African American	**2**	1	0.4245	0.2511	2.8569	0.09
Caucasion	**3**	1	-0.6626	0.4057	2.6674	0.10
Sex	**1**	1	0.05	0.09	0.27	0.60
CoronaryArteryDisease	**1**	1	0.136	0.12	1.29	0.25
Diatetes Mellitus	**1**	1	-0.055	0.09	0.30	0.57
Smoker	**1**	1	0.2142	0.1161	3.4043	0.06
Atrial Fibrillation	**1**	1	-0.0353	0.1418	0.0618	0.80
Depression	**1**	1	0.2709	0.1278	4.4907	0.03

Analysis of Maximum Likelihood Estimates

Parameter		DF	Estimate	Standard Error	Wald Chi-Square	Pr > ChiSq
Carotid Stenosis	**1**	1	-0.0764	0.1883	0.1647	0.68
Seizure History	**1**	1	0.5404	0.1660	10.6044	0.001
Hypertension	**1**	1	-0.1555	0.1357	1.3133	0.25
Hyperlipidemia	**1**	1	0.1672	0.1088	2.3588	0.12

Odds Ratio Estimates

Effect	Point Estimate	95% Wald Confidence Limits	
NCC yes vs. no	24.59	15.21	39.75
AGE	0.99	0.98	1.00
Hispanic vs. Asian/Other	1.04	0.51	2.11
African American vs. Asian/Other	1.38	0.60	3.19
Non-white vs. Asian/Other	0.46	0.13	1.58
Male vs. female	1.11	0.75	1.63
CAD yes vs. no	1.31	0.82	2.10
Diabetes Mellitus yes vs. no	0.89	0.60	1.32

Analysis of Maximum Likelihood Estimates					
Parameter	**DF**	**Estimate**	**Standard Error**	**Wald Chi-Square**	**Pr > ChiSq**
Smoker yes vs. no			1.53	0.97	2.42
Atrial Fibrillation yes vs. no			0.93	0.53	1.62
Depression yes vs. no			1.71	1.04	2.83
Carotid Stenosis yes vs. no			0.85	0.41	1.79
Seizure history yes vs. no			2.94	1.53	5.64
Hypertension yes vs. no			0.73	0.43	1.24
Hypelipidemia yes vs. no			1.39	0.91	2.14

Table 12

Demographics of Probable NCC Patients with Acute Stroke and Prior Stroke

Probable NCC Patients w/ Acute Stroke			**Probable NCC Patients w/ Prior Stroke**	
	N=40		**N=86**	
Gender	Number	%	Number	%
Males	14	35%	31	36%
Females	26	65%	55	64%
Age Groups	Number	%	Number	%
20-39 years	2	5.0%	3	3.4%
40-59 years	13	32.5%	15	17.4%
60-79 years	17	42.5%	39	45.3%
80-99 years	8	20.0%	29	33.7%
Ethnicity	Number	%	Number	%
Hispanic	34	85.0%	77	89.5%
African American	1	2.5%	2	2.3%
Caucasian	1	2.5%	1	1.1%
Asian	2	5.0%	2	2.3%
Other	1	2.5%	3	3.4%
Unknown	1	2.5%	1	1.1%
Country of Birth/Birth Place				
	Number	%	Number	%
Mexico	27	67.5%	58	67.4%
USA	5	12.5%	14	16.2%

El Salvador	1	2.5%	3	3.4%
Korea	2	5.0%	0	0.0%
Unknown	5	12.5%	3	0.0%
Guatemala	0	0.0%	5	5.8%
Peru	0	0.0%	1	1.1%
Haiti	0	0.0%	1	1.1%
Europe	0	0.0%	1	1.1%
Religion	Number	%	Number	%
Catholic	23	57.0%	58	67.4%
Non Denom.	11	27.0%	22	25.5%
Other Christian	2	5.0%	3	3.4%
Jehovah's Witness	1	2.5%	0	0.0%
Unknown	2	5.0%	1	1.1%
Other	1	2.5%	1	1.1%
SDA*	0	0.0%	1	1.1%

*(SDA=Seventh Day Adventist)

Table 13

Clinical Risk Factors in Probable NCC Patients with Acute and Previous Stroke

Probable NCC Patients w/ Acute Stroke N=40				**Probable NCC Patients w/ Prior Stroke N=86**		
Clinical Risk Factor	(Number) %			(Number) %		
	Yes	**No**	**Unknown**	**Yes**	**No**	**Unknown**
Hypertension	(33) 83%	(6) 15%	(1) 2%	(61) 71%	(24) 28%	(1) 1%
Diabetes	(18) 45%	(21) 53%	(1) 2%	(33) 38%	(53) 62%	(0) 0%
CAD*	(16) 40%	(23) 56%	(1) 2%	(34) 40%	(50) 58%	(2) 2%
Hyperlipidemia	(14) 35%	(26) 65%	(0) 0%	(19) 22%	(67) 78%	(0) 0%
Smoking	(6) 15%	(33) 83%	(1) 2%	(13) 15%	(71) 83%	(2) 2%
Atrial Fibrillation	(6) 15%	(33) 83%	(1) 2%	(12) 14%	(73) 85%	(1) 1%
Seizures	(5) 13%	(34) 85%	(1) 2%	(10) 12%	(76) 88%	(0) 0%
Depression	(5) 13%	(34) 85%	(1) 2%	(12) 14%	(73) 85%	(1) 1%
Carotid Stenosis	(1) 2%	(38) 95%	(1) 2%	(1) 1%	(84) 98%	(1) 1%

*(CAD=-Coronary Artery Disease)

Table 14

Location of Infarcts in Probable NCC Cases

	Probable NCC Patients w/ Acute Stroke N=40		**Probable NCC Patients w/ Prior Stroke N=86**	
Location	Number	%	Number	%
Basal Ganglia	9	22.5%	22	25.5%
Lacunar	0/9	0.0%	16/22	72.7%
Two or more Locations	8	20.0%	19	22.0%
Lacunar	6/8	75.0%	16/19	84.2%
Unspecified locations	3	7.5%	11	12.7%
Frontal Lobe	1	2.5%	9	10.4%
Parietal Lobe	2	5.0%	8	9.3%
MCA Infarct	1	2.5%	6	6.9%
Cerebellum	2	5.0%	3	3.4%
Pons	6	15.0%	3	3.4%
Temporal Lobe	3	7.5%	3	3.4%
Occipital Lobe	1	2.5%	2	2.3%
Thalamus	4	10.0%	0	0.0%

APPENDIX A

Institutional Review Board Approval

University of California Los Angeles
11000 Kinross Avenue, Suite 211
Los Angeles, CA 90095-1694

http://ohrpp.research.ucla.edu
GC-IRB: (310) 825-7122
M-IRB: (310) 825-5344

APPROVAL NOTICE
New Study

DATE:	6/21/2013
TO:	JENNIFER GARLAND SCHOOL OF NURSING
FROM:	ALISON MOORE, MPH, MD Chair, SGIRB
RE:	IRB#13-000858 Examining the Relationships Among Neurocysticercosis, Stroke, and Presenting Symptoms

The UCLA Institutional Review Board (UCLA IRB) has approved the above-referenced study. The UCLA IRB's Federalwide Assurance (FWA) with Department of Health and Human Services is FWA00004642 (IRB00004474).

Submission and Review Information

Type of Review	Expedited Review
Approval Date	6/18/2013
Expiration Date of the Study	6/17/2014
Funding Source(s)	

Regulatory Determinations

– **Expedited Review Category 5** - The UCLA IRB determined that the research meets the requirements for expedited review per 45 CFR 46.110 category 5.

– **Waiver of Informed Consent** - The UCLA IRB waived the requirement for informed consent under 45 CFR 46.116(d) to obtain records.

Important Note: Approval by the Institutional Review Board does not, in and of itself, constitute approval for the implementation of this research. Other UCLA clearances and approvals or other external agency or collaborating institutional approvals may be required before study activities are initiated. Research undertaken in conjunction with outside entities, such as drug or device companies, are typically contractual in nature and require an

APPENDIX B

Study Site Authorization Agreement

White Memorial Medical Center

Adventist Health

1720 Cesar E. Chavez Ave.
Los Angeles, CA 90033
213-268-5000

WHITE MEMORIAL MEDICAL CENTER AUTHORIZATION AGREEMENT

Name of Institution or Organization Providing IRB Review (Institution A):

UCLA

Name of Institution Relying on the Designated IRB (Institution B):

Western Institutional Review Board (WIRB) on behalf of White Memorial Medical Center
FWA #: IRB00000533

The Officials signing below agree that Western Institutional Review Board (WIRB) may rely on the designated IRB for review and continuing oversight of its human subject research described below. *[check one]*

(___) This agreement applies to all human subjects' research covered by Institution B's FWA.

(__X_) This agreement is limited to the following specific protocol(s):
Name of Research Project: Title: Examining the Relationships Among Neurocysticercosis, Stroke, and Presenting Symptoms

Principal Investigator: Jennifer Garland, PhD (c.) UCLA IRB: PRE#13-001167

Project Site: WMMC
(___) Other *[Please Describe]*

The review performed by the designated IRB will meet the human subject protection requirements of Institution B's OHRP-approved FWA. The IRB at Institution/ Organization A will follow written procedures for reporting its findings and actions to appropriate officials at Institution B. Relevant minutes of IRB meetings will be made available to Institution B upon request. Institution B remains responsible for ensuring compliance with the IRB's determinations and with the Terms of its OHRP- approved FWA. This document must be kept on file by both parties and provided to OHRP upon request.

Signature of Signatory Official

_____ Date: 05/08/2013

Print Full Name: Michael Jordan, RN MSN, MBA

Institutional Title: Clinical Research Program Coordinator

V 17Jul09

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APPENDIX C

Data Abstraction Form

CT BRAIN WO CONTRAST Abstraction Form

(Estimated abstract time per scan: 5-10 mins)

<table>
<tr><td colspan="3">Adm to ED? Y N Admitted to Hosp? Y N</td></tr>
<tr><td colspan="3">Date of scan: Hospital Service: IP OP AC PSYCH</td></tr>
<tr><td colspan="3">Did patient die on this admission? Y N</td></tr>
<tr><td colspan="3">Age: Gender: M F Interpreting Radiologist:</td></tr>
<tr><td colspan="3">LOS in days</td></tr>
<tr><td colspan="3">Country of Birth: Country of Residence:</td></tr>
<tr><td colspan="3">Race/Ethnicity (as defined by hospital):</td></tr>
<tr><td colspan="3">Zip code: Occupation: Insurance:</td></tr>
<tr><td colspan="3">Religion:</td></tr>
<tr><td colspan="3">Presenting signs/symptoms:</td></tr>
<tr><td>Hx of smoking? YES NO</td><td>Evidence of HTN? YES NO</td><td>Hx of SZ YES NO</td></tr>
<tr><td>Hx of AFIB YES NO</td><td>Hx of Depression YES NO</td><td>Hx of Carotid Stenosis Y N</td></tr>
<tr><td>Hx of HLD? YES NO</td><td>Evidence of Diabetes? YES NO</td><td>Hx MI/CABG/CAD/ACS? YES NO</td></tr>
<tr><td colspan="3">Evidence of (neuro) cysticercosis on CT brain WO contrast?</td></tr>
<tr><td colspan="3">Evidence of acute infarct or hemorrhage? If yes, Isch or Hem?</td></tr>
<tr><td colspan="3">Evidence of previous infarct or hemorrhage? If yes, Isch or Hem?
Location:</td></tr>
<tr><td colspan="3">Final diagnosis at discharge:</td></tr>
<tr><td colspan="3">tPA given? Y N</td></tr>
</table>

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