Risk factors for encephalitis and death from West Nile virus infection

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SUMMARY

We conducted a nested case-control study to determine potential risk factors for developing encephalitis from West Nile virus (WNV) infection. Retrospective medical chart reviews were completed for 172 confirmed WNV cases hospitalized in Houston between 2002 and 2004. Of these cases, 113 had encephalitis, including 17 deaths, 47 had meningitis, and 12 were fever cases; 67% were male. Homeless patients were more likely to be hospitalized from WNV compared to the general population. A multiple logistic regression model identified age [odds ratio (OR) 1·1, $P < 0.001$], history of hypertension, including those cases taking hypertension-inducing drugs (OR 2·9, $P = 0.012$), and history of cardiovascular disease (OR 3·5, $P = 0.061$) as independent risk factors for developing encephalitis from WNV infection. After adjusting for age, race/ethnicity (being black) (OR 12·0, $P < 0.001$), chronic renal disease (OR 10·6, $P < 0.001$), hepatitis C virus (OR 23·1, $P = 0.0013$), and immunosuppression (OR 3·9, $P = 0.033$) were identified as risk factors for death from WNV infection.

INTRODUCTION

Since St. Louis encephalitis virus was first recognized in Houston in 1964, the area has remained endemic with flavivirus activity [1]. In 2002, a West Nile virus (WNV) outbreak was identified in Houston with 105 human cases reported to the Centers for Disease Control and Prevention (CDC). Nationally, 4156 WNV-positive cases were reported [2].

The vast majority of human cases of WNV infection are asymptomatic [3]. Milder infections can exhibit flu-like symptoms, which can go undiagnosed as WNV infection. Approximately one out of 140 infected persons will develop neuroinvasive disease, including meningitis and encephalitis [4].

Elderly patients are at highest risk for encephalitis and death [3, 5–8]. Other than advanced age, risk factors for developing neuroinvasive disease from WNV have not been clearly identified. Factors such as hypertension and cerebrovascular disease that disrupt the cerebral endothelium thereby promoting virus entry and replication in the blood–brain barrier

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endothelium, as well as other factors that can increase the level and duration of viraemia, such as immunosuppression and immune senescence, have been hypothesized as potentially important risk factors for neuroinvasive disease [6].

This paper presents a nested case-control study that was conducted in order to identify potential risk factors for developing encephalitis among hospitalized WNV-positive cases reported to the City of Houston and Harris County health authorities between 2002 and 2004.

MATERIALS AND METHODS

Human surveillance and case identification

Identification of a WNV-positive dead blue jay in the Houston area in mid-June of 2002 prompted health officials to alert area physicians of virus activity. Physicians who suspected WNV infection in their patients were encouraged to send CSF or sera to the City of Houston Department of Health and Human Services (HDHHS) laboratory. Patients who tested positive for anti-WNV IgM antibodies by enzyme-linked immunosorbent assay or ELISA [3, 6] were reported to one of the two health departments that serve the Houston metropolitan area, HDHHS or Harris County Public Health and Environmental Services (HCPHES), depending on the patient's residence. Some specimens were also sent to CDC for confirmatory testing by ELISA and plaque reduction neutralization testing (PRNT). Probable cases with unconfirmed laboratory results (positive CSF or sera at HDHHS laboratory but negative ELISA or PRNT at CDC) during the acute phase of illness had a convalescent serum tested for WNV by haemagglutination-inhibition (HI) at the Department of Pathology, University of Texas Medical Branch (UTMB) [1]. All probable cases tested by UTMB had negative test results and were excluded from this study. Other cases excluded included those not hospitalized for their illness or hospitalized outside of the Houston metropolitan area. All WNV laboratory-confirmed hospitalized cases in the Houston area were selected for medical chart abstractions and included in this study.

Study population

The population for Harris County, which includes the city of Houston, is more than 3·4 million people [9].

Non-Hispanic whites make up 42·1% of the population, followed by 32·9% of Hispanic or Latino origin, 18·5% black, and 5·1% Asian.

Clinical data collection

Chart abstractions were conducted by the local city and county health departments as part of their investigation of a reportable disease. A chart abstraction form was created to collect demographic and clinical information. Cases were classified using a case definition derived from Sevjar et al. [10] into the following groups:

(1) encephalitis/meningoencephalitis/ encephalomyelitis (WNE);
(2) meningitis (WNM);
(3) viral syndrome with fever (WNF).

Data analysis

We conducted a nested case-control study using data from the chart abstractions on hospitalized WNV patients. Data was entered into Epi-Info 2002 (CDC, Atlanta, GA, USA) and analysed using the statistical functions of Epi-Info 2002, Number Cruncher Statistical Software (NCSS, Kaysville, UT, USA), and STATA statistical software (StataPress, College Station, TX, USA). Comorbidities and social histories were identified in the medical history section of the medical record as reported by the patient or surrogate and recorded by the attending physician. Pre-existing hypertension was defined as previous diagnosis of hypertension by a physician, including those under treatment. Cardiovascular disease (CVD) was defined as reporting a history of any of the following: CVD, coronary artery disease, history of myocardial infarction, and other heart or vascular conditions that affect function. Immunosuppression was defined as having at least one of the following immune-suppressing conditions: HIV, cancer (not in remission >5 years), organ transplantation, diabetes, and chronic alcohol abuse. Chronic alcohol abuse was determined either through physician diagnosis in the medical record or if the patient self-reported >3 drinks per day or >15 per week. Current drug use was determined either by self-report of the patient or by positive urine drug screen. Death was attributed to WNV if the death occurred during the patient's hospitalization for their WNV illness. A Kruskal–Wallis one-way analysis of variance (ANOVA) on ranks was performed to

determine differences in the median age distribution between case classifications (WNF, WNM, WNE, and WNE deaths). Based on this result along with other clinical parameters (severity of illness, length of hospitalizations), WNE patients, including deaths, were identified as 'cases', and WNM and WNF cases were identified 'controls'.

Univariate analysis on demographic variables and comorbidities was conducted to determine risk factors for developing encephalitis. Model-building strategies were used to develop a logistic regression model that best described the effects of the covariate on the outcome of encephalitis. All variables on univariate analysis with a P value of <0.25 were entered into a logistic regression model. At the multiple regression level, variables with a P value of >0.10 were excluded using a backward step-wise approach. The final model included all variables with a P value of <0.10. The Hosmer–Lemeshow goodness of fit statistic [11] was used to assess the fit of the final model. Univariate analysis was also conducted to determine risk factors for death, but due to the small sample size of deaths, logistic regression could not be modelled. As an alternative, variables identified as significant on univariate analysis ($P \leqslant 0.05$) were adjusted for age.

This study was approved by the University of Texas Health Science Center Committee for the Protection of Human Subjects (HSC-SPH-03-039) and complied with the United States Health Insurance Portability and Accountability Act.

RESULTS

Descriptive epidemiology

The first human case of WNV-associated illness in Houston was confirmed on 23 July 2002. Between 2002 and 2004, 172 hospitalized cases from the Houston area were confirmed positive for WNV and selected for inclusion in this study. Of these 172 cases, 88 were identified in 2002, 49 in 2003, and 35 in 2004.

Of the 172 cases, 113 (66%) were classified as WNE, 47 (27%) as WNM, including four cases with myelitis, and 12 (7%) as WNF. Of the 12 WNF cases, all presented with fever and severe headache, however, eight did not have a lumbar puncture, so we were unable to determine if they had pleocytosis in the CSF, potentially classifying them as meningitis cases. There were 17 deaths, all encephalitic, associated with this outbreak (case fatality rate 10%). Dates of illness onset for all cases ranged from 15 June (2003 case) to
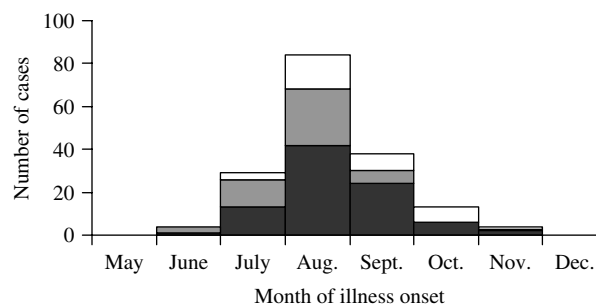

Fig. Epidemic curve of Houston cases of West Nile virus between 2002 and 2004 by date of onset of illness and year of presentation. ■, 2002; ▨, 2003; □, 2004.

16 November (2004 case) (Fig.). Seventy-one percent of cases were hospitalized in August and September. Median number of days hospitalized were as follows: WMF, 3 days; WNM, 4 days; WNM with myelitis, 21·5 days; and WNE, 10 days.

Men represented 67% of all patients, 71% of WNE cases, and 59% of deaths (Table 1). White, non-Hispanic patients represented the majority of cases (55%), followed by black (21%), Hispanic (23%) and Asian or Middle Eastern (2%). Black patients represented 47% of the deaths (Fisher exact two-tailed $P = 0.01$).

The median age at onset of all hospitalized cases was 54 years, with a range of 5 months to 95 years. Seven (4%) cases occurred in children aged $\leqslant 20$ years. Median age for the fatal cases was 75 years (range 47–95 years); median age for WNE non-fatal cases was 61·5 years (range 9–88 years); median age for WNM was 39 years (range 5 months to 67 years); median age for WNF was 47 years (range 1–69 years). An ANOVA on ranks revealed a significant difference in median ages based on grouping by outcome ($P < 0.001$). The multiple-comparison z value test showed a significant difference ($P < 0.05$) in median ages between (1) the WNF and both WNE and WNE deaths, and (2) WNM and both WNE and WNE deaths. There was no significant difference in ages between WNM and WNF cases.

Comorbidities

Pre-existing hypertension was the most commonly reported comorbidity, with 50% of patients reporting pre-existing hypertension, including 65% of all WNE patients (OR 7·4, 95% CI 3·4–17·1, $P < 0.001$), and 82% of WNE deaths (OR 5·4, 95% CI 1·4–30·1, $P = 0.005$) (Table 2).

Table 1. *West Nile virus-positive patient demographics, Houston, 2002–2004*

Case characteristics	All cases, $n = 172$ (%)	Attack rate†	WNE deaths ($n = 17$) No. (%)	WNE deaths OR (95% CI)	All WNE ($n = 113$) No. (%)	WNM/WNF ($n = 59$) No. (%)	Risk of developing WNE OR (95% CI)
Female	56 (33)	3·28	7 (41)	1·5 (0·5–4·7)	33 (29)	23 (39)	Reference
Male	116 (67)	6·85	10 (59)	0·7 (0·2–2·2)	80 (71)	36 (61)	1·5 (0·8–3·0)
Age (yr)							
0–19	7 (4)	0·65	0	0	4 (4)	3 (5)	Reference
20–44	41 (24)	2·95	0	0	8 (7)	33 (56)	0·2 (0·03–0·2)*
45–64	64 (37)	9·48	5 (29)	0·3 (0·1–1·1)*	45 (40)	19 (32)	1·8 (0·4–8·7)
⩾65	60 (35)	23·73	12 (71)	Reference	56 (50)	4 (7)	10·5 (1·7–64·1)*
Race/ethnicity							
White, non-Hispanic	95 (55)	6·56	7 (41)	Reference	62 (55)	32 (54)	Reference
Black	36 (21)	5·73	8 (47)	3·6 (1·2–11·1)*	25 (22)	11 (19)	1·2 (0·5–2·6)
Hispanic	39 (23)	3·48	2 (12)	0·7 (0·1–3·5)	24 (21)	15 (25)	0·8 (0·4–1·8)
Asian/Asian Indian	2 (1)	1·15	0	0·0	1 (1)	1 (2)	0·5 (0·03–8·4)
Homeless	10 (6)	100·0	2 (12)	2·5 (0·2–13·9)	9 (8)	1 (2)	5·0 (0·7–223·7)

WNE, Encephalitis/meningoencephalitis/encephalomyelitis; WNM, meningitis; WNF, viral syndrome with fever; OR, odds ratio; CI, confidence interval.

† Attack rates per 100 000 population using 2000 census data for Harris County and homeless population estimates [13].

* Significant, $\alpha = 0.05$.

Forty-seven (27%) patients reported a history of diabetes mellitus, including 32% of all WNE patients (OR 2·0, 95% CI 0·9–4·9, $P = 0.07$), and 53% of WNE deaths (OR 3·5, 95% CI 1·1–11·0; Fisher exact two-tailed $P = 0.02$). Of the 47 diabetics, 36 (77%) also had a history of hypertension. Diabetes was reported by 44% of Hispanic patients, 39% of black patients, and 17% of white, non-Hispanic patients.

Other comorbidities identified included CVD (23%), history of cancer but not including those in remission >5 years (9%), stroke (7%), chronic renal insufficiency (8%), hypothyroidism (8%), hepatitis C virus (4%), HIV (2%), hepatitis B virus (2%), pregnancy (2%), and heart transplantation (1%). All 14 patients with a history of chronic renal insufficiency, 74% patients with CVD, and 75% of patients with a history of stroke also reported pre-existing hypertension. There were 88 (51%) patients who reported an immunosuppressing condition, including 58% of WNE patients (OR 2·4, 95% CI 1·2–4·8, $P = 0.009$) and 76% of WNE deaths (OR 3·5, 95% CI 1·0–15·1, $P = 0.03$).

Social histories

Use of tobacco products was reported by 37% of patients (Table 2). Chronic alcohol abuse was reported for 35 (20%) cases; 31 of the 35 cases (89%) were males. History of recent illicit drug use was identified in 25 (15%) patients. The most commonly identified illicit drugs included central nervous system (CNS) stimulants such as crack/cocaine (14/25) and amphetamines (3/25) (not mutually exclusive). Other drugs identified include heroin/opiates (5/25), benzodiazepines (4/25), and marijuana (11/25). Eight patients had more than one illicit drug either reported or found by urine drug screen. Five (3%) patients reported a recent history of intravenous drug use. One death tested positive by urine drug screen for both cocaine and amphetamines, and two deaths had a history of intravenous drug use. There was a significant difference between the median ages of those who reported either illicit drug or alcohol abuse (median 49 years) and those with no history of abuse (median 58 years) when tested by Kruskal–Wallis one-way ANOVA on ranks ($P = 0.02$). The difference between the median age of the four illicit drug or alcohol abusers who died (median 54 years) and non-abusers who died (median 76 years) was also significant ($P = 0.036$).

Ten patients reported being homeless, including nine WNE patients (two fatal cases) and one WNM with viral myelitis; all homeless patients were male. The homeless population in Houston

Table 2. *Findings from social and medical histories, Houston, 2002–2004*

Case characteristics	All cases, n = 172 (%)	WNE deaths (n = 17)		All WNE, n = 113 (%)	WNM/WNF, n = 59 (%)	Risk of developing WNE OR (95% CI)
		No. (%)	OR (95% CI)			
Social histories						
Tobacco use	63 (37)	9 (53)	2·1 (0·7–6·6)	42 (37)	21 (36)	1·1 (0·5–2·2)
Chronic alcohol abuse	35 (20)	11 (65)	10·0 (3·0–35·6)**	27 (24)	8 (14)	2·0 (0·8–5·5)
Illicit drug use†	25 (15)	4 (24)	2·0 (0·4–7·2)	16 (14)	9 (15)	0·9 (0·4–2·5)
CNS stimulants (crack/ cocaine or amphetamines)	14 (8)	2 (12)	1·6 (0·2–8·2)	10 (9)	4 (7)	1·3 (0·4–6·1)
Heroin/opiates	5 (3)	2 (12)	6·8 (0·5–62·7)	3 (3)	2 (3)	0·8 (0·1–9·6)
Marijuana	11 (6)	2 (12)	2·2 (0·2–11·9)	4 (4)	7 (12)	0·3 (0·1–1·0)*‡
Injecting drug user	5 (3)	2 (12)	6·8 (0·5–62·7)	4 (4)	1 (2)	2·1 (0·2–106·6)
Comorbidities						
History of hypertension	86 (50)	14 (82)	5·4 (1·4–30·1)**	74 (65)	12 (20)	7·4 (3·4–17·1)**
History of hypertension including drug-induced hypertension	94 (55)	14 (82)	4·4 (1·2–24·5)*	79 (70)	15 (25)	6·8 (3·2–14·9)**
Cardiovascular disease	39 (23)	8 (47)	3·6 (1·1–11·3)*	36 (32)	3 (5)	8·7 (2·5–46·1)**
Diabetes	47 (27)	9 (53)	3·5 (1·1–11·0)*	36 (32)	11 (19)	2·0 (0·9–4·9)
Immunosuppressing condition§	88 (51)	13 (76)	3·5 (1·0–15·1)*	66 (58)	22 (37)	2·4 (1·2–4·8)**
Chronic lung disease	19 (11)	4 (24)	2·9 (0·6–10·9)	16 (14)	3 (5)	3·1 (0·8–17·1)
Cancer (excluding those in remission >5 years)	16 (9)	6 (35)	7·9 (1·9–29·4)**	14 (12)	2 (3)	4·0 (0·9–37·6)
Stroke	12 (7)	2 (12)	1·9 (0·2–10·4)	11 (10)	1 (2)	6·3 (0·9–273·8)
Chronic renal disease	14 (8)	6 (35)	10·0 (2·4–39·4)**	14 (12)	0	OR undefined**
Hypothyroidism	14 (8)	4 (24)	4·5 (1·0–18·7)*	11 (10)	3 (5)	2·0 (0·5–11·7)
Hepatitis C virus	7 (4)	3 (18)	8·1 (1·1–52·1)*	6 (5)	1 (2)	3·3 (0·4–152·1)
Hepatitis B virus	4 (2)	1 (6)	3·2 (0·1–41·5)	3 (3)	1 (2)	1·6 (0·1–84·5)
HIV	4 (2)	1 (6)	3·2 (0·1–41·5)	2 (2)	2 (3)	0·5 (0·04–7·3)
History of head trauma	4 (2)	0	0·0 (0·0–14·4)	4 (4)	0	OR undefined
Pregnancy	3 (2)	0	0·0 (0·0–22·8)	0	3 (5)	0·0 (0·0–1·2)

WNE, Encephalitis/meningoencephalitis/encephalomyelitis; WNM, meningitis; WNF, viral syndrome with fever; OR, odds ratio; CI, confidence interval.

† More than one illicit drug was either reported or found by urine drug screen in nine patients.

‡ Does not retain statistical significance after controlling for age ($P = 0.47$).

§ Defined as history of cancer (not including those in remission >5 years).

* Significant at $\alpha = 0.05$; ** significant at $\alpha = 0.01$; HIV, diabetes mellitus, organ transplantation, or history of chronic alcohol abuse.

is estimated to be 10 000 [12]. When compared to the general population, homeless individuals were almost 21 times more likely to be hospitalized for WNV illness (OR 21·0, 95% CI 10·4–40·8, $P < 0.001$), and 29 times more likely to be hospitalized for encephalitis (OR 29·4, 95% CI 13·9–59·8, $P < 0.001$).

Risk factors for encephalitis and death

Significant risk factors for developing encephalitis identified on univariate analysis included advanced age, being male, history of hypertension or taking hypertension-inducing drugs (CNS stimulants), history of CVD, stroke, chronic renal disease, and immunosuppressing conditions (Table 2). The final logistic regression model identified the following independent risk factors significant ($P < 0.10$) for encephalitis: advanced age (OR 1·1, $P < 0.001$), history of hypertension or taking hypertension-inducing drugs (OR 2·9, $P = 0.012$), and history of CVD (OR 3·5, $P = 0.061$) (Table 3). Interaction terms were entered into the model and were not found to be statistically significant. The Hosmer–Lemeshow

Table 3. *Logistic regression findings: significant ($\alpha = 0 \cdot 1$) independent risk factors for developing encephalitis*

Outcome = WNE	P value	OR	95% CI
Age	<0·001	1·1	1·03–1·1
History of hypertension including drug-induced hypertension	0·012	2·9	1·3–6·8
History of cardiovascular disease	0·061	3·5	0·9–13·3

WNE, Encephalitis/meningoencephalitis/encephalomyelitis; OR, odds ratio; CI, confidence interval.

goodness-of-fit test statistic was 6·12 ($P > 0·6338$), suggesting that the model is a good fit.

Univariate analysis identified the following significant ($\alpha = 0·05$) risk factors for death: advanced age, race/ethnicity (black), chronic alcohol abuse, history of hypertension or taking hypertension-inducing drugs, diabetes, at least one immunosuppressing condition, cancer within 5 years, chronic renal disease, hypothyroidism, and hepatitis C virus infection (Table 2). When age-adjusted, race/ethnicity (black) (OR 12·0, 95% CI 3·03–47·4, $P < 0·001$), chronic renal disease (OR 10·6, 95% CI 2·7–41·4, $P < 0·001$), hepatitis C virus (OR 23·1, 95% CI 3·4–157·3, $P = 0·0013$), and immunosuppression (OR 3·9, 95% CI 1·1–13·6, $P = 0·033$) remained significant. Due to the small sample size of the outcome (death), logistic regression modelling could not be performed.

DISCUSSION

The outbreak of WNV in the late summer of 1999 in New York City represented the first known occurrence of WNV in the Western Hemisphere [5, 13]. In 2002, WNV was first detected in the Houston metropolitan area [1]. Based on previous seroprevalence estimates that one out of 140 WNV-infected persons will develop meningoencephalitis [4] we can roughly estimate that at least 22 000 Houstonians became infected between 2002 and 2004. Our research presents the only known large-scale case-control study that attempts to identify risk factors for developing encephalitis from WNV infection.

There are several striking similarities and differences between the Houston and New York City outbreaks. Both Houston and New York City found similar percentages of patients with encephalitis (66% and 63% respectively), and similar case-fatality rates (10% and 12% respectively) [5]. In New York City, median age of hospitalized cases was 71 years, with a median age for deaths being 81·5 years. Among the hospitalized Houston patients, the median age was younger for all cases (54 years) and for deaths (75 years). An age-related difference between the two outbreaks could partly be attributed to a larger prevalence of illicit drug use (15% of Houston cases and no reported cases in New York City) and chronic alcohol abuse (20% of Houston cases compared to 2% of New York City cases) in the Houston study population. Cocaine and amphetamines can cause an increase in systemic blood pressure, with prolonged abuse contributing to chronic hypertension and CVD [14]. Chronic alcohol abuse can lead to both immunosuppression and hypertension [14, 15]. Of the 49 cases who reported illicit drug use or chronic alcohol abuse, the median age was 49 years, compared to a median age of 58 years for those who were non-abusers. Of four deaths who reported illicit drug use or chronic alcohol abuse, the median age was 54 years, compared to a median age of 76 years among the 13 non-abusers. Clinicians should note that a history of illicit drug or alcohol abuse could increase the risk of a patient being hospitalized for WNV infection at a younger age. Interventions aimed at risk reduction in this population are important, particularly since they are also at greater risk for homelessness and increased mosquito exposures.

An interesting and important finding from the study of the Houston cases was the identification of homeless persons being at increased risks for hospitalization from WNV infection compared to the general population. Homeless individuals can be placed at greater risk for infection due to their increased outdoor exposures to mosquitoes. Also, all homeless individuals in this outbreak were male and had a history of chronic alcohol abuse, also placing them at greater risk. Targeted interventions, including educational campaigns and distribution of mosquito repellent, might help reduce the risk of infection in these higher risk populations.

In New York City, age of ≥75 years and diabetes mellitus were both shown to be independent risk factors for death [5]. In the Houston WNV patient population, diabetes was not found to be a significant risk factor for encephalitis on logistic regression, but was found to be a significant risk factor for death on univariate analysis. After adjusting for age, this association decreased in significance ($P = 0·054$). Of

the 17 deaths, 14 had pre-existing hypertension and nine were diabetics; all but one of the diabetics had a history of hypertension.

Diabetic patients are twice as likely to have hypertension when compared to the general population [16–18]. Patients with both diabetes and hypertension generally have increased morbidity and mortality. Diabetes and hypertension have both been shown to be independent risk factors for increased permeability of the blood–brain barrier, although the mechanisms that contribute to endothelial dysfunction have not been discovered [18–20]. Increased permeability of the blood–brain barrier during the viraemia period of WNV infection could possibly lead to increased susceptibility of the patient to neuroinvasive disease.

In the logistic regression model, age, a history of hypertension or hypertension-inducing drugs, and history of CVD were identified as significant independent risk factors for encephalitis, which is the first time a study has been able to better support the hypothesis that hypertension as well as a compromised heart or vascular system are associated with increased risk for severe disease from WNV infection. Since encephalitis cases typically presented with altered mental status, accurate medical histories could not always be obtained. This could have lead to an underreporting of pre-existing hypertension or CVD in these cases, potentially increasing the significance of both of these variables as risk factors for encephalitis.

A limitation worth noting is the chance for false associations due to multiple comparisons in the logistic regression modelling, although model-building strategies were used to help avoid this. Another limitation in this study was the potential for not identifying other risk factors for neuroinvasive disease since all cases included in the analysis were hospitalized predominantly for meningitis and encephalitis. The risk factors evaluated in this study are co-morbidities that are typically associated with poor underlying health, which in turn can increase the risk for hospitalization. Additionally, the vast majority of people infected with WNV are not hospitalized, including those who might have restricted access to care or are considered to be of low socioeconomic status. These factors can create a bias in the selection of cases and controls, however, we attempted to minimize this by ensuring enrolment of all identified confirmed hospitalized cases. Since increased age can be associated with immunosuppression [21] and age and sex can be associated with greater risk for hypertension [22], a case-control study using age-and sex-matched WNV-positive asymptomatic controls would be ideal; however, a large and costly sero-prevalence approach would be needed to capture enough controls to achieve this type of study.

On univariate analysis, blacks had a higher risk of dying compared to other race/ethnicities. Of the eight blacks who died, median age was 62 years, seven had at least one immunosuppressing condition, seven had a history of hypertension, and two were homeless. Since the sample size of deaths in this study is small, this increased proportion could be related to chance. Collecting additional information on deaths attributed to WNV over time would allow us to determine whether there is a true disparity between blacks and other race/ethnicities.

We identified seven children hospitalized from WNV in Houston between 2002 and 2004. WNV illness in children has not been well documented in the literature, and little is known about the risk factors for encephalitis. None of the children identified with WNV encephalitis in Houston had a history of immunosuppression; one child had a history of previous head trauma. Because of the small sample size of children among the Houston cases, we were limited in our ability to make inferences about this disease in children. Assessing potential risk factors for severe disease will be critical in understanding the mechanisms of pathogenesis in children, which would allow for the development of potential intervention measures for those placed at higher risk.

DECLARATION OF INTEREST

None.

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