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An investigation of depression and fatigue post West Nile virus infection.

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An Investigation of Depression and Fatigue Post West Nile Virus Infection

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Abstract

Introduction: The purpose of this study was to examine depression and fatigue in individuals with a seropositive confirmed history of West Nile virus (WNV) infection.

Methods: The South Dakota State Epidemiologist sent 218 letters inviting residents with a diagnosis of WNV to participate in the study. Forty-five subjects were tested. An occupational therapist and a physical therapist met with each participant to assess performance parameters, including depression and fatigue levels. Subjects (n=42) completed the Revised Center for Epidemiologic Studies Depression Scale (CES-D) during the assessment. The Modified Fatigue Impact Scale (MFIS) was sent to participants as a follow-up questionnaire, and 29 were returned.

Subjects were placed within one of three diagnosis groups: West Nile Fever (WNF), West Nile Neuroinvasive Disease (WNND) and WNV without fever or neuroinvasive disease (clinical/ unspecified).

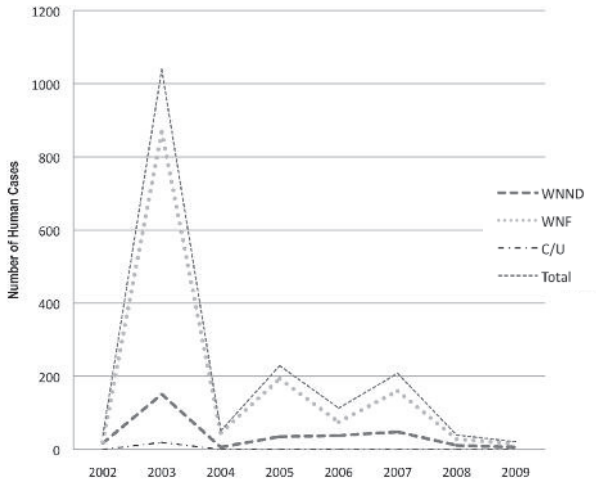
Results: Frequency of those reporting low risk of depression was similar between diagnosis groups (each approximating 75 percent). Depression severity differences were noted, with subjects diagnosed with WNND more likely to report "severe" risk for depression. Low correlations between depression and overall fatigue, depression and cognitive fatigue, and depression and psychosocial fatigue indicators were found. There was little if any correlation between depression and physical fatigue indicators. Mean CES-D scores for subjects between 13 to 18 months post infection fell within the mild-moderate risk for depression category.

Conclusions: Identifying depression risk is useful for patient referral purposes and may help minimize symptoms of depression correlated with fatigue, especially following hospitalization for WNV infection.

Introduction

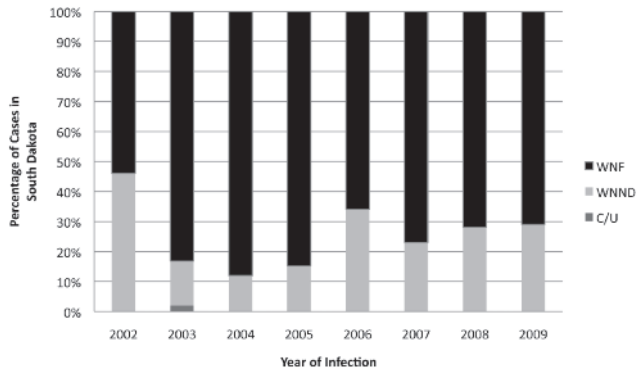
The first case of West Nile virus (WNV) infection in the United States was reported in New York City in 1999.[1,2] Not long thereafter, the number of confirmed cases of WNV infections escalated from 66 in 2001 to 4,156 in 2002.[2,3] In South Dakota, the first 37 cases of WNV infection emerged in 2002, and by 2003, South Dakota reported 1,039 confirmed human cases. That was exceeded only by Colorado (2,947) and Nebraska (1,942) in national reported human cases during 2003.[2] These cases in South Dakota represented 10.5 percent of the confirmed national cases in 2003. As health education and mosquito control efforts have increased, the incidence of human-confirmed West Nile virus cases have declined by astonishing measures. In 2009, South Dakota reported only 21 (3.1 percent) of the 663 confirmed national cases (Figure 1).[2,4]

Figure 1.
Annual confirmed cases of West Nile infection in South Dakota (including diagnostic classifications).



The majority of WNV cases are mild in nature, and it is suspected that a large number (up to 80 percent) of individuals infected with WNV do not know they have been infected with the virus.[5] National statistics estimate about 20 percent of cases result in a condition called West Nile fever (WNF), while less than 1 percent progress to a more serious form called West Nile neuroinvasive disease (WNND).[6] In South Dakota, among those with a seropositive confirmed case of the infection between 2002 and 2009, an average of 74.5 percent experienced WNF, while an average of 25.3 percent reported WNND and 0.2 percent were confirmed clinical cases with unspecified symptoms (C/U) (Figure 2).

Figure 2.
Annual confirmed cases of West Nile infection in South Dakota (percentage of distribution by diagnosis).



Subjective reports from individuals with a diagnostic history of WNV include complaints of extreme fatigue.[7,8] Watson, et al.[8] determined that 96 percent of those subjects with WNF reported fatigue lasting a median of 36 days immediately following diagnosis. Lobe, et al.[9] reported patients with WNV infection experienced symptoms of fatigue up to an average of four months post-diagnosis and that normalization of fatigue levels took longer in patients with WNND than without.

Depression is also a symptom commonly reported by individuals infected with WNV.[7] According to Carson, et al.,[10] of those individuals infected with WNV, 24 percent experienced moderate-to-severe depression, while only 10 percent of the sample had experienced depression prior to their infection. This finding may suggest that individuals infected with WNV are at greater risk for experiencing clinical depression. According to Murry, et al.,[11] 31 percent of study subjects reported new onset of depression a year after diagnosis, and 75 percent of these cases reported Center for Epidemiologic Studies Depression Scale (CES-D) scores which fell within the mild to severe depression risk categories.[12] Sixty-five percent of these new-onset cases of depression had a diagnosis of WNV encephalitis. Murry, et al.[11] stated subjective reports of personality changes were common for individuals after WNV infection. Anxiety and depression symptoms have also been positively correlated with a history of WNV infection.[7] In addition to anxiety and depression, individuals have also reported progressive changes in mood and aggression, as well as increased sensitivity and decreased socialization following WNV infection.[7]

Based upon a review of the literature, there is evidence to suggest that those with a history of WNV have an elevated risk of both depression and fatigue. During the scheduling and planning stages of this study, evidence from the literature was supported by subjective reports of commonly occurring fatigue, mood changes, memory deficits and depression in this sample. The purpose of this study was to further examine the prevalence of and relationship between fatigue and depression in individuals with a confirmed history of WNV infection.

Methods

Subjects

Seropositive confirmed cases of WNV infection between 2002 and 2006 and residing (at time of infection) in one of nine southeastern South Dakota counties were identified by the South Dakota Department of Health. The southeastern region of South Dakota was selected based upon a reasonable participant proximity to the testing site. To maintain individual confidentiality, letters were sent by the state epidemiologist's office with investigator contact information for those interested in participating in this study.

The South Dakota State Epidemiologist sent 218 letters inviting subjects with a seropositive confirmed diagnosis of WNV infection to participate in this study. Of those individuals invited, 74 responded to the invitation to participate (33.9 percent) and 59 were scheduled for testing (27.1 percent of population). Respondents were screened to meet the following inclusion criteria: a seropositive confirmed case of WNV infection, English-speaking, age 18 or older, and no major medical diagnosis since infection (e.g. stroke, heart attack, Parkinson's disease, multiple sclerosis, cancer and the like).

Ten scheduled individuals did not show up for their testing appointment, and four subjects cancelled or could not be rescheduled, resulting in assessments for 45 of 59 scheduled

individuals (20.5 percent of the total population). Three subjects were eliminated from data analysis due to conditions that may have confounded results. Subject demographics were as follows: 55 percent male and 45 percent female; 14.3 percent with encephalitis; 7.1 percent with meningitis; 7.1 percent with encephalomeningitis; 52.4 percent with fever only; and 19.0 percent reporting symptoms without fever; 28.6 percent were hospitalized for more than 24 hours (Table 1). Subject age ranged between 35 and 81 years, with a mean age of 54.4 years (SD=10.7 years). Months since WNV diagnosis ranged from 13 to 53 months post infection, with an average time passage of 38.6 months since diagnosis (SD=15.4 months).

Table 1.
Participant Characteristics (n=42)

Variable		Number	Percentage (percent)
Gender			
	Male	23	(54.8)
	Female	19	(45.2)
Age			
	Mean years ± SD	54.4 ± 10.7	
	≥ 65 years, No. (percent)	6	(14.3)
	Age range	35-81	
Diagnosis			
	West Nile fever	22	(52.4)
	West Nile neuroinvasive disease	12	(28.6)
	Clinical/Unspecified	8	(19.0)
Hospitalization			
	No	28	(66.7)
	Yes (> 24 hours)	12	(28.6)
	Yes (< 24 hours)	2	(4.8)
Time from Diagnosis to Testing			
	13-18 months	9	(21.4)
	19-36 months	7	(16.7)
	37-48 months	1	(2.4)
	49-60 months	22	(52.4)
	Missing	3	(7.1)

Instruments

Center for Epidemiologic Studies Depression scale (CES-D),[12] the Brief Fatigue Inventory (FI)[13] and the Modified Fatigue Impact Scale (MFIS)[14] were used for the purpose of investigating fatigue and depression. The CES-D is a self-report assessment consisting of 20 questions related to thoughts and feelings within the past week. The FI consists of nine items rated zero ("none") to 10 ("severe") addressing current fatigue levels and surveying the extent to which fatigue interferes with daily activities, ability to socialize and enjoyment of life. The MFIS is a questionnaire consisting of 21 specific items to assess the effects of fatigue. Results from the MFIS are reported as a total fatigue score with physical, cognitive and psychosocial functioning subscales.

Procedures

Between October 2007 and March 2008, respondents met with a physical therapist and an occupational therapist for a 2.5-hour comprehensive assessment session, during which time functional tests were administered to measure strength, coordination, balance, endurance, memory, cognition, activities of daily living and occupational participation, fatigue and depression levels. All tested subjects completed the CES-D and the FI during their established assessment time, and the MFIS was sent to participants as a follow-up questionnaire to gather more sensitive information about fatigue measures than the FI. Twenty-nine participants returned the MFIS questionnaire.

Participants were given the option to share medical and rehabilitation records relevant to their course of treatment for WNV infection. All participants agreed to share these medical records. Information provided by subjects was validated through released medical records. Participants were assured their information would remain confidential, and all individuals signed consent forms approved by the university IRB. All participants were offered a $30 prepaid credit card as travel compensation. As a follow up to each participant's visit, individualized reports were generated by the occupational therapist and physical therapist and were sent to each participant and their primary care providers, upon participant consent.

Data Analysis

The study design was a non-experimental, cross-sectional analysis. Subjects were classified into three diagnostic groups based upon chart reviews: (1) West Nile Fever (WNF): those subjects whose medical chart confirmed the presence of fever (n=22); (2) West Nile Neuroinvasive Disease (WNND): those subjects whose medical chart confirmed the presence of meningitis, encephalitis, or anterior horn cell involvement resulting in paresis or paralysis (n=12); and (3) C/U: absence of fever or neurological expression in the medical records despite seropositive confirmation of WNV infection (n=8).

Spearman's rho was used to determine any correlation that existed between CES-D depression scores and MFIS total fatigue scores as well as between CES-D and MFIS physical, cognitive and psychosocial subscale scores. A cross tabulation was performed between CES-D scores and the three WNV diagnosis categories.

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Figure 3.
Distribution of subjects within diagnostic classifications into depression risk categories.

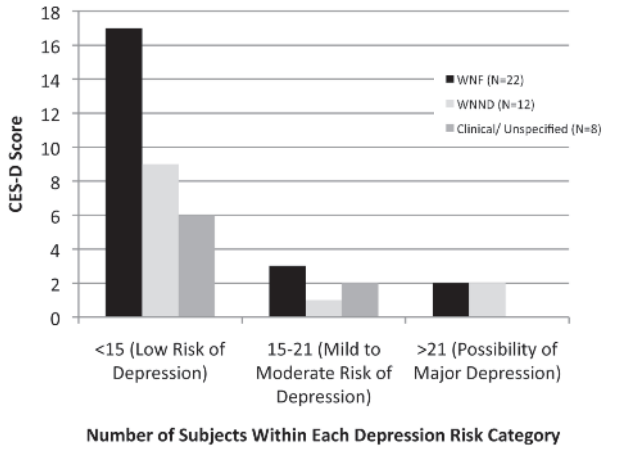
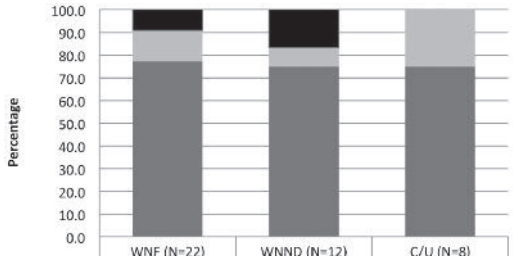


Figure 4/ Table 2.
Percentage distribution of subjects within diagnostic classifications, defined by depression risk categories



	WNF (N=22)	WNND (N=12)	C/U (N=8)
>21 (Possibility of Major Depression)	9.1	16.7	0.0
15-21 (Mild to Moderate Risk of Depression)	13.6	8.3	25.0
<15 (Low Risk of Depression)	77.3	75.0	75.0

Participants were also grouped by time passage following diagnosis (Table 1), and a one-way ANOVA was administered to determine if trends in depression severity were observed in groups based upon period of time post infection. LSD post hoc tests were run to determine levels of significance, with a level of significance set at 0.05. Data were analyzed with Statistical Package for Social Sciences (SPSS) version 17.0.

Results

Frequency of those reporting low risk of depression was relatively consistent between diagnostic groups (75.0 percent of those in WNF and C/U groups and 77.3 percent of those in the WNND group). Participants with WNND showed the highest probability for major depression risk (16.7 percent), followed by subjects with WNF (9.1 percent; Figures 3 and 4; Table 2).

A low correlation15 between depression and fatigue was determined with r =.338 (p=.031; Table 3). There was low correlation between depression indicators and MFIS cognitive fatigue indicators (r=.376, p=.015) as well as between depression and psychosocial indicators r =.348 (p=.026). There was little if any[15] correlation between depression and physical fatigue indicators.

The mean difference in CES-D scores between those 13 to 18 months post infection was significant (p=.016) when compared to those individuals 19 to 36 months post infection. Mean CES-D score for those in the 13 to 18 month post infection group was 17.1, placing this group's mean within the "mild-moderate" risk for depression score range. All other group means fell within the "low" risk score range (Table 4).

Discussion

While it is true that the incidence of WNV infection has declined as preventive mosquito control measures have intensified, those with a history of WNV continue to live with the consequences of infection through activity limitations, changes in cognitive functioning, and a compromised quality of life.[7-12]

Table 3.
Relationship between depression (CES-D scores) and fatigue (MFIS scores) indicators as reported by individuals post West Nile virus infection

	Depression and Total Fatigue	Depression and Physical Subscale	Depression and Cognitive Subscale	Depression and Psychosocial Subscale
Correlation Coefficient	.338	.215	.376	.348
Sig. (2 tailed)	.031*	.177	.015*	.026*
.00-.25 little if any correlation		.26-.49 low correlation		

** indicates significant with p<.05*
Munro's descriptive terms for the strength of correlations coefficients are used[15(p235)]

Table 4.
Risk of depression as examined by time passage post diagnosis

Months Post Diagnosis	N	Mean CES-D Score	Score Interpretation
13-18	9	17.1	Mild to Moderate Risk of Depression
19-36	7	5.9	Low Risk of Depression
37-49	5	8.0	Low Risk of Depression
50-60	18	10.7	Low Risk of Depression
Total	39	11.0	Low Risk of Depression

Depression and fatigue were among the most prevalent subjectively reported symptoms in this study. Practitioners should be aware that individuals with a history of WNV infection, most specifically those with a diagnosis of WNND, may be at greater risk for severe depression and may benefit from patient monitoring or referral at early sign of depression.

Nearly every participant in this study reported pervasive fatigue impacting one or all of the following: endurance levels, changes in an individual's ability to engage in work and activities of daily living, cognitive functioning and psychosocial participation. Over and again, tested individuals confided their work capacity was impaired and that they had quit very meaningful activities because they no longer had the endurance, stamina or ability to sustain a sufficient activity level. The low but statistically significant correlation between cognitive and psychosocial fatigue factors and depression gives cause for concern that the limitations imposed by fatigue may contribute to depression for some individuals post WNV infection.

These authors were surprised to observe that there was little to no correlation between the physical fatigue subscale and depression. However, the MFIS physical fatigue questions probe respondents for high levels of physical debilitation, which did not appear to be problematic for this sample population.

Primary care provider awareness of the risks for depression associated with WNV infection may guide physician decision-making when monitoring patients post WNV infection. This research suggests patients with a history of neuroinvasive forms of WNV and those patients who are 13 to 18 months post infection demonstrate the greatest risk for depression. The primary care provider may desire to perform a depression survey tool such as the Patient Health Questionnaire (PHQ-9)[9] when a patient hospitalized with WNV infection is discharged. This screen may be intermittently repeated during the next 18 months of follow-up. Such monitoring will give the primary care provider a discharge point of reference and aid the provider in identifying patients with depression post infection.

It is fortunate that fewer patients are currently affected by this viral infection. However, providers should be mindful of the chronic impact of infection, which may extend years beyond hospitalization. With this awareness, physicians should be prepared to refer patients to mental health professionals, occupational therapists or other health professionals, depending upon the apparent source of depression. It is in the provider's best interest to understand the benefits of monitoring fatigue levels and depression for these patients in order to address health from a holistic perspective.

The present study had several limitations. First, the study design did not include an age-matched control group. The sample size was small, and there was inequitable subject grouping after diagnostic categorization was completed, with fewer individuals in the C/U group (n=8) as compared to the WNF group (N=22). It can be said that this inequitable distribution is reflective of, though not proportionate to, the inequitable distribution of diagnostic cases of WNV, with the cases of WNF largely outnumbering the cases of WNND and C/U. Subjects were limited to southeastern South Dakota as a matter of proximity to the testing site. A choice of moving the testing site, had it been practically and financially possible, may have drawn a larger population sample. Furthermore, a low response rate to the MFIS mailing (69.0 percent), reduced the data set for fatigue information for an already small sample size.

Next, because subjects did not complete CES-D and MFIS results immediately following their infection confirmation, results were only useful in providing point-in-time data to identify potential trends between subjects. Longitudinal individual improvements or increasing debilitation could not be determined by this type of study design. Finally, subjects may be self-selecting in that those invited participants with the greatest impairments, least mobility or limited access to transportation may not have been able to travel to the assessment clinic for testing; for instance, there were no subjects with a diagnosis of acute flaccid paralysis, the most devastating physical expression of WNND. Addressing these limitations in future studies could provide better generalized results.

In conclusion, this study offers meaningful insight to primary care providers working with individuals with a history of WNV infection. Providers should be mindful that patients who have a history of neuroinvasive disease may be at risk for severe depression, that individuals 13 to 18 months post infection show an elevated risk for depression and that fatigue and depression are among the most frequently reported subjective complaints associated with long-term functional outcomes following WNV infection.

Providers should use this information to improve screening, to appropriately refer, and to monitor patients in the event of newly diagnosed infections.

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