Answering the CDC's Call for Universal HIV Testing: Assesing the Impact on a Tertiary Care Referral Center via a Blinded Seroprevalence Study

Margaret Hoffman-Terry MD, FACP
Lehigh Valley Health Network, Margaret.Terry@lvhn.org

K Nadeem Ahmed MD
Lehigh Valley Health Network

Joseph L. Yozviak DO, FACP
Lehigh Valley Health Network, joseph.yozviak@lvhn.org

Sherrine Eid MPH
Lehigh Valley Health Network, Sherrine.Eid@lvhn.org

Timothy J. Friel MD
Lehigh Valley Health Network, Timothy.Friel@lvhn.org

See next page for additional authors

Published In/Presented At

Hoffman-Terry, M., Ahmed, K., Yozviak, J., Eid, S., Friel, T., Pacella, K., & Rhodes III, L. (2008, October 25-28). *Answering the CDC's call for universal HIV testing: assessing the impact on a tertiary care referral center via a blinded seroprevalence study.* Poster presented at: The 48th Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) and the 46th Annual Infectious Disease Society of America (IDSA) Annual Meeting, Washington, DC.

Authors

Margaret Hoffman-Terry MD, FACP; K Nadeem Ahmed MD; Joseph L. Yozviak DO, FACP; Sherrine Eid MPH; Timothy J. Friel MD; Kimberly A. Pacella; and Luther Rhodes III MD

Poster #H-470
48th ICAAC
Washington, DC
October 25-28, 2008
Contact information:
Margaret.Terry@LVH.com

Answering the CDC's Call for Universal HIV Testing: Assessing the Impact on a Tertiary Care Referral Center via a Blinded Seroprevalence Study

Margaret Hoffman-Terry, MD, K. Nadeem Ahmed, MD, Joseph Yozviak, DO, Sherrine Eid, MPH, Kimberly Pacella, Timothy Friel, MD, Luther V. Rhodes, III, MD. Lehigh Valley Hospital and Health Network, Allentown, PA

ABSTRACT:

Objective: To obtain an accurate picture of the HIV epidemic in the inpatient and outpatient population served by a large tertiary care referral center by conducting a blinded seroprevalence study.

Methods: 601 outpatients (OP) and 399 inpatients (IP) were included. All leftover blood samples in the central laboratory were de-identified and then consecutively tested for HIV via ELISA with confirmatory Western blot and HCV via Abbott's Microparticle Enzyme ImmunoAssay with RIBA performed for those not meeting the CDC's recommended signal to cut-off ratio of 9.9 for true antibody positivity. Sampling was stratified to be representative of the age groups served by this 3 site, 986 bed hospital system. OPs were oversampled in an attempt to more accurately represent the epidemic in the community served by the hospital system.

Results: Of the 9 who were confirmed HIV positive, 7 (78%) were IP compared to 2 (22%) OP (Fisher's exact test p=.024). HIV positive pts. were 5.34 times as likely to be IP as OP (OR 5.34, CI [1.11,25.78]). 5 (56%) were male compared to 4 (44%) female (Fisher's exact test p>.05). 8/9 cases fell in the 25-54 range, with the largest subgroup being those pts. between 45-54 years of age (4/9). 6/9 were from the urban area immediately surrounding the hospital sites, 1 from the suburbs, 1 from a rural community, and 1 from a distant city served by the network. Only 3 HCV co-infected cases were found-all IP, from an urban area, and between the ages of 47-50. One case of HIV was confirmed in the 65-80 year range-beyond the age recommended for testing by the CDC.

Conclusions: The IP positivity rate of 1.75% is well above the 1% rate felt necessary for cost effective testing of a population and supports the current CDC recommendation to offer testing to all patients as they access healthcare in an attempt to identify new cases. The OP rate of 0.33% was surprisingly low and points to the need to develop novel strategies for identifying HIV cases among those not regularly accessing the healthcare system.

INTRODUCTION:

HIV is typically symptomatic for only a few weeks after acute infection and then silent for 10-12 years until the immune system is shattered and Acquired Immunodeficiency Syndrome (AIDS) ensues. The Center for Disease Control currently indicates that there are more than 1 million Americans living with HIV infection. More strikingly, the CDC estimates that approximately one quarter of these individuals have never been tested for HIV and are therefore unaware of their status and that this population causes 54 to 70% of new infections[1]. In years past the CDC had recommended targeted testing of high-risk populations, a policy under which we have continued to see approximately 50,000 new infections annually in the US, with many patients presenting late in the course of their disease. Since 2006 the CDC has recommended Universal Testing. Under this policy, HIV screening is recommended for patients ages 18-64 in all health-care settings after the patient is notified that testing will be performed unless the patient declines (opt-out screening). Those at high risk for HIV infection should be screened for HIV at least annually. Separate written consent and prevention counseling should not be required[2].

Because of shared modes of transmission, 25-90% of HIV patients, depending on the subpopulation being studied, are co-infected with chronic Hepatitis C [3,4]. The metamorphosis of HIV from a rapidly fatal to a chronically manageable disease means that persons with HIV now go on to die from illnesses other than traditional opportunistic infections. The diseases they most commonly die from now across the US are cancers followed by end stage liver disease related to hepatitis C[5], and the Lehigh Valley has followed this trend. From 2000-2005, 58% of deaths in our HIV clinic occurred in the 35% of our HIV patients who were co-infected, with 29.5% of deaths the result of end stage liver disease secondary to HCV[6]. To evaluate the extent of one epidemic without evaluating the other seemed imprudent since the two are so closely intertwined.

The implications of Universal HIV Testing are manifold. Who will fund this testing? How do we change state laws to comply with these recommendations? Who will care for these patients this age of healthcare cost constraints with fewer HIV providers available every year? We sought to examine the following question: How many HIV cases will be identified in this manner and how many will be coinfected with HCV?

OBJECTIVE:

To establish a precise seroprevalence of Hepatitis C Virus (HCV) and Human Immunodeficiency Virus (HIV) in the community serviced by Lehigh Valley Hospital and Health Network (LVHHN) including the hospital and the Lehigh Valley Physicians' Practice which serves a primarily uninsured/ underinsured population. This provided us with 2 key pieces of information: the actual number of persons infected with HIV alone and the degree of co-infection with both viruses. Furthermore, we analyzed differences in age, gender, and zip code (as surrogate marker of residence) in an effort to understand these intertwined epidemics.

METHODS:

The strategy was to indiscriminately screen 1000 patients between the ages of 18 and 80 who have leftover blood after having labs drawn in the LVHHN. Based on a 99% confidence interval with a 5% margin for error, an adequate sample size is 1000 subjects. All red top tubes drawn for basic metabolic profiles were sequentially allocated beginning at 0600 on February 6, 2008 until 400 inpatients (220 females and 180 males) and 600 outpatients (368 females and 232 males) including those seen in the emergency department were sampled. The sample were stratified into age and sex groups based on admission statistics of the previous year (Table 1). Proportions of admissions of each age group were determined based on inpatient or outpatient status. Inpatient was defined as anyone in a bed at 12 AM midnight at all LVH sites, including all medical, surgical, psychiatry, hospice and transitional skilled units, including observation admissions. Outpatient visits were determined to be emergency department visits, clinics, same day surgery, cancer patients receiving services at the Cancer Center's Multi-purpose area, and home hospice.

The age groups for each sex were: Group I –ages 18-24, Group II –ages 25-34, Group III –ages 35-44, Group IV –ages 45-54, Group V –ages 55-64 Group VI –ages 65-80. Specimens were chosen in an anonymous and unlinked fashion to protect the confidentiality of the patients. Neither the researchers nor the patients are able to track the results to the sample source. Since each specimen is no longer traceable or linked to its source, the researchers in this project were not obligated to notify the patients of the results as that would be impossible after each specimen was de-identified. The protocol was reviewed by our hospital ethicist and approved by the Institutional Review Board and HIPAA compliance officer.

The LVHHN laboratory tested all blood received during the time period indicated only after a medical technician had removed all identifiers. As each specimen was received and frozen, a master list of the last four digits of the medical record number was recorded to avoid duplication until sampling was complete. Each specimen was then assigned a unique consecutive case number starting at 100 through 1100, with this number entered independently in a second database. In this second database with the newly assigned case number, demographic information including age, sex, Zip code, and site of collection (Inpatient, ER, and Outpatient) was recorded. The first database containing the last 4 digits of the medical record number was deliberately destroyed in the presence of our hospital's compliance officer upon completion of sampling and prior to any serologic testing to assure blinding and prevent association of any kind between medical record number and sample result.

The frozen blood samples were thawed and tested consecutively for antibodies to HIV and HCV using the Enzyme Linked Immunosorbent Assay (ELISA). A confirmatory Western blot was performed for all positive HIV ELISAs. HCV testing was done using Abbott's Microparticle Enzyme ImmunoAssay with RIBA performed for those not meeting the CDC's recommended signal to cut-off ratio of 9.9 for true antibody positivity. The specimen requirements of ELISA are minimal so there was no need for additional blood draws. The results of the diagnostic test (ELISA) were then recorded in the second database devoid of medical record numbers. Many HIV and HCV studies, including a recent Philadelphia study of HIV and a Houston study of HCV, had been successfully conducted in this blinded manner [7,8].

Variables: To compare the demographic and epidemiologic data between populations in the LVHHN versus other urban/rural areas regionally and nationwide, the following variables were identified for all samples tested:

- Age
- Gender
- Zip code of residence
- Source of blood sample-outpatient, ER, inpatient
- Infection with HIV and /or HCV

Analytic Methodology: The stated indicators were analyzed by the LVHHN Health Studies Department using univariate and multivariate analyses in SPSS 15.0 statistical software. T test and Pearson's Chi-square analyses were conducted on the provided data examining differences in infection rates by region, age, and gender. In addition to this, associations were examined using Pearson's correlation. Descriptive statistics on demographics and overall results using Poisson lower and upper bounds were reported. The Poisson limits identify plausible ranges and reflect the 95% confidence intervals. Seroprevalence was determined by the equation; P=x/n, where x is the number of positive samples and n is the overall sample.

RESULTS:

1000 patients were included in this HIV/HCV seroprevalence study. Nine were confirmed HIV positive and twenty-eight cases were confirmed HCV positive with three confirmed co-infected with HCV and HIV. The outpatient setting was over sampled in an attempt to capture as many individuals and potential cases not currently in the system.

Of those were HIV positive, nearly 78% were inpatients compared to 22% outpatient (Fisher's Exact Test p=.024). HIV positive patients were 5.34 times as likely to be inpatients than outpatients (OR 5.34, CI [1.11,25.78]). The distribution of men and women was not statistically significant. Nearly 56% were men compared with 44% HIV positive women (Fisher's exact test p>.05).

RESULTS (cont.):

The overwhelming majority of HIV positive cases were between the ages of 25-54, with the largest subgroup being those patients between 45-54 years of age; 11.1% of HIV positive cases were between the ages of 65-80. 6/9 were from the urban area immediately surrounding the hospital sites, 1 from the suburbs, 1 from a rural community, and 1 from a distant city served by the network. Only 3 HCV co-infected cases were found-all IP, from an urban area, and between the ages of 47-50.One case of HIV was confirmed in the 65-80 year range-beyond the age recommended for testing by the CDC.

Men were 2.2 times more likely to be HCV positive than women (OR 2.229 CI [1.033,4.810]). There was no difference in the distribution of HCV-infected patients with regards to being inpatient or outpatient (Pearson's χ^2 p>.05). HCV cases tended to be more scattered between urban, suburban and rural areas with HIV cases concentrated in urban areas.

Table 1: LVHHN Hospital Discharge Data Dec. 2005 – Nov. 2006

LVHHN Hospital Discharge Data		
Inpatient		
Age Group	**Male**	**Female**
Group I 18-24	9	18
Group II 25-34	13	32
Group III 35-44	23	34
Group IV 45-54	37	40
Group V 55-64	39	39
Group VI 65-80	58	57
Total	180	220
Outpatient		
Age Group	**Male**	**Female**
Group I 18-24	25	35
Group II 25-34	32	48
Group III 35-44	42	69
Group IV 45-54	48	83
Group V 55-64	40	65
Group VI 65-80	45	68
Total	232	368

Table 2. HIV Breakdown by Age Group

	Age Group						Total
	18-24	25-34	35-44	45-54	55-64	65-80	
HIV Positive	0% (0)	33.3% (3)	11.1% (1)	44.4% (4)	0% (0)	11.1% (1)	100% (28)
Total	8.5% (85)	12.5% (125)	16.8% (168)	20.8% (208)	18.3% (183)	23.1% (231)	100% (1000)

Table 3. HCV Breakdown by Age Group

	Age Group						Total
	18-24	25-34	35-44	45-54	55-64	65-80	
HCV Positive	3.6% (1)	3.6% (1)	21.4% (6)	60.7% (17)	7.1% (2)	3.6% (1)	100% (28)
Total	8.5% (85)	12.5% (125)	16.8% (168)	20.8% (208)	18.3% (183)	23.1% (231)	100% (1000)

CONCLUSION:

Establishing the seroprevalence of HIV and HCV by ensuring anonymity and unlinked data serves as a model in assessing overall disease burdens in the Lehigh Valley, as it has in other communities and large cities. Given the growing disease burden of these synergistic infections, it is of paramount importance to accurately determine seroprevalence and identify cases early in their disease course when treatment will be most efficacious. The IP positivity rate of 1.75% is well above the 1% rate felt necessary for cost effective testing of a population and supports the current CDC recommendation to offer testing to all patients as they access healthcare in an attempt to identify new cases. The fact that 7/9 HIV positives were found in inpatients in this day and age when our usual inpatient census is 1 and most patients live for decades only being cared for in the outpatient arena was surprising. Eight of nine patients would have been diagnosed under Universal Testing guidelines, though one of our 9 cases was found in a patient over 64 years of age who would have thus fallen outside the CDCs recommended age window for HIV testing. The OP rate of 0.33% was surprisingly low and points to the need to develop novel strategies for identifying HIV cases among those not regularly accessing the healthcare system.

REFERENCES:

1) Marks G. Crepaz N. Janssen RS. Estimating sexual transmission of HIV from persons aware and unaware that they are infected with the virus in the USA. AIDS. 20(10):1447-50, 2006 Jun 26.
2) Branson BM, Handsfield HH, Lampe MA, taylor, RS et al. Revised recommendations for HIV testing of adults, adolescents, and pregnant women in health-care settings. Morbidity & Mortality Weekly Report. Recommendations & Reports. 55(RR-14):1-17; quiz CE1-4, 2006 Sep 22.
3) Alter, MJ, Margolis, HS, et al. Recommendations and Reports: Recommendations for Prevention and Control of Hepatitis C Virus (HCV) Infection and HCV-Related Chronic Disease. Morbidity and Mortality Weekly Report (MMWR), Centers for Disease Control and Prevention. Oct 1998; 47/RR19):1-39.
4) Sherman KE, Rouster SD, et al. Hepatitis C Virus Prevalence Among Patients Infected with Human Immunodeficiency Virus: A Cross-sectional Analysis of the US Adult AIDS Clinical Trials Group. Clin Infect Dis. 2002;34:831-837.
5) Tedaldi E, Baker R, Moorman A, Alzola C, et al. Influence of Coinfection with HCV on Morbidity and Mortality Due to HIV Infection in the Era of Highly Active Antiretroviral Therapy. Clin Infect Dis. 2003; 36: 363-367.
6) Hoffman-Terry M, Kimmel S, Smith A, Mannino J. Medical and Psychiatric Morbidity and Mortality in in HIV/ HCV co-infected and HIV mono-infected patients in the era of HAART. Abstract CDB0333. XVI International AIDS Conference. Toronto, Canada, 2006.
7) Brady KA, Berry S, Gupta R, Weiner M. Seasonal Variation in Undiagnosed HIV Infection on the General Medicine and Trauma Services of Two Urban Hospitals. J Gen Int Med. 2005 apr; 20 (4): 324-30.
8) D'Souza G, Arafat R, Hwang L, Cunningham C et al, Cross-sectional Survey of the Extent and Indicators of HCV Infection in Houston Dept. of Health and Human Services' Sexually Transmitted Disease Clinics. J Viral Hepatitis 2003 Mar; 10 (2): 134-140.
9) McQuillan GM, Alter MJ, Moyer LA, Lambert SB, Margolis HS. A population based serologic study of hepatitis C virus infection in the United States. In Rizzetto M, Purcell RH, Gerin JL, Verme G, eds. Viral Hepatitis and Liver Disease, Edizioni Minerva Medica, Turin, 1997, 267-70.

LEHIGH VALLEY HOSPITAL AND HEALTH NETWORK

ANCC MAGNET RECOGNITION