Comorbid Conditions, Treatment, and Health Maintenance in Older Persons with Human Immunodeficiency Virus Infection in New York City

Sanjiv S. Shah,1,4 Joseph P. McGowan,1,4 Cheryl Smith,5,6 Steve Blum,2,4 and Robert S. Klein1,4
1Division of Infectious Diseases and 2Department of Medicine, Bronx-Lebanon Hospital Center, 3Division of Infectious Diseases, Department of Medicine, Montefiore Medical Center, and 4Department of Medicine, Albert Einstein College of Medicine, Bronx, and 5Department of Medicine, North General Hospital, and 6Mount Sinai School of Medicine, New York, New York

We retrospectively examined comorbid conditions and health maintenance in 198 patients aged ≥55 years who attended 3 New York City human immunodeficiency virus (HIV) clinics between 1 January 1990 and 30 June 1998. Annual influenza and pneumococcal vaccinations within 5 years were given in 82% and 86% of patients, respectively. Among 57 women, 79% had a Papanicolaou smear within 1 year, and 53% had a mammogram within 2 years. Of 165 patients who received care after 1 July 1996, 147 (89%) had comorbid conditions (mean number of conditions, 2.4), and 133 (81%) received HIV-unrelated medications (mean number of medications, 2.7). Receipt of highly active antiretroviral therapy, its discontinuation because of toxicity, and having an undetectable HIV load were not related to comorbid conditions or use of concurrent medications. Comorbid conditions and use of concurrent HIV-unrelated medications need not adversely affect treatment of HIV-infected older individuals, but increased attention to health maintenance may be necessary.

Among individuals reported to have AIDS in the United States through December 2000, ∼11% were ≥50 years old at the time of diagnosis [1]. By the mid-1990s, the rate of increase in AIDS cases in this age group was among the highest in the nation [2]. Older age at time of HIV infection correlates with shorter AIDS-free survival time and survival after AIDS diagnosis, regardless of risk factors [3–8].

Since HAART became widely available in 1996, the prognosis for patients with HIV infection has improved significantly [9]. However, the effectiveness of HAART depends on access to, receipt of, and adherence to complex medical regimens [10]. Practitioners may be reluctant to prescribe complex combination therapy to their older patients, especially when these patients may have comorbid conditions that require long-term use of additional medications, because the pill burden may be perceived as complicating necessary adherence to a strict medication regimen [11]. HIV-infected individuals ≥55 years old have nearly 4 times more chronic comorbid conditions than do those <45 years old [12]. As survival from HIV infection improves in response to the availability of more effective therapy, unrelated medical conditions are likely to assume increasing importance as causes of morbidity and mortality in persons with HIV infection. However, poorer prognosis due to more rapid HIV disease progression among older HIV-infected patients may have an impact on practitioner adherence to health maintenance screening guidelines for these individuals [13].

To determine the characteristics of disease due to HIV infection in older individuals, including comorbid
conditions and the use of antiretroviral therapies, we conducted
a retrospective review of clinical experience at our institutions.
The objectives of this study were (1) to describe the demo-
graphic characteristics, HIV risk behaviors, and clinical dis-
orders of older persons with HIV infection who received pri-
mary care at 3 inner-city HIV clinics; (2) to assess possible
associations of comorbid conditions and treatment for such
conditions with receipt of, benefit from, and adverse reactions
to antiretroviral therapies; and (3) to determine the level of
routine health maintenance not necessarily related to HIV in-
festation.

METHODS

Outpatient medical records for all HIV-infected patients ≥55
years old who had ≥2 clinic visits (≥1 visit after the patient
reached age 55 years) between 1 January 1990 and 30 June 1998
at 3 New York City hospital HIV clinics (Montefiore Medical
Center, Bronx-Lebanon Hospital Center, and Mount Sinai
Medical Center) were reviewed. Patients were selected by age
at the most recent clinic visit from databases that recorded all
registered visits at each clinic. Data on demographic charac-
teristics, HIV risk behaviors, substance abuse, stage of HIV
disease (including CD4⁺ lymphocyte count and plasma HIV-
1 load, measured by Roche Amplicor PCR), use of antiretroviral
therapy, long-term (>6 months) use of HIV-unrelated med-
cication, chronic (>6 months duration) comorbid conditions,
use of prophylaxis for *Pneumocystis carinii* pneumonia (PCP),
and health maintenance screening (including documentation
of mammography within 2 years and annual Papanicolaou
smears for women, history of pneumococcal and influenza
vaccinations, measurement of serum total cholesterol level, tu-
berculin skin testing, and mental status evaluation) were ab-
stracted from standardized data-collection forms. If a stan-
dardized neurocognitive examination or an evaluation by a
neurologist or psychiatrist had been documented, the patient
was considered to have had a formal mental status evaluation.
A patient was considered to have used antiretroviral or other
medications if there was evidence in the medical record that
medication was prescribed and no evidence that the patient
was not taking it.

The 3 clinics each had equivalent policies regarding care of
HIV-infected patients, including documentation of health
maintenance procedures, neurocognitive assessment, risk be-
haviors for HIV acquisition, prescription of HIV-related and
-unrelated medications, and presence of comorbid conditions.
Published guidelines were used for determining adherence to
standard practices for health maintenance procedures, vacci-
nations, and use of PCP prophylaxis [14–16]. The interval since
the health care screening was calculated as the time elapsed
between the screening and the most recent recorded visit to
the clinic. It was assumed that tests or procedures for which
there was no documentation had not been done.

The use and tolerability of HAART, which became available
in early 1996, was evaluated in a subgroup consisting of 165
patients who received care at 1 of the 3 clinics after 1 July 1996.
US Department of Health and Human Services guidelines for
the use of HAART were published in April 1998 [17]. HAART
was defined as the combination of nucleoside analogue reverse-
transcriptase inhibitors (NRTIs) with a nonnucleoside analogue
reverse-transcriptase inhibitor, an HIV-1 protease inhibitor
(P1), or both.

Categorical data were analyzed by the χ² test or Fisher’s exact
test, and continuous data were analyzed by t tests or the non-
parametric Kruskal-Wallis test. The study was approved by the
institutional review board for the protection of human subjects
at each institution.

RESULTS

One hundred ninety-eight HIV-infected patients ≥55 years of
age were seen at 1 of the 3 clinics during the study period.
There were no significant differences between patient charac-
teristics at the clinic sites. Fifty-seven patients (29%) were
women. The median age of all patients was 59 years (range,
55–82 years). Ninety-eight patients (50%) were non-Hispanic
black, and 95 patients (48%) were Hispanic (table 1). Assess-
ment of risk factors for HIV acquisition revealed that the only
risk factor was heterosexual contact with a high-risk partner
(a person known to be infected with HIV, a commercial sex
worker, or, for women, a bisexual man) for 95 patients (47%)
and was injection drug use for 59 (30%); 11 patients (6%) were
men who had sex with men (MSM) and had no other risk
factors; and 19 (10%) had no reported risk factor. Twelve pa-
tients (6%) had multiple risk factors. The median CD4⁺ lym-
phocyte count at first clinic visit was 239 cells/mm³. Sixty-seven
percent (132) of the patients had received a diagnosis of AIDS
by the most recent clinic visit, and 58% (76) of these had an
AIDS-defining clinical condition. The most common AIDS-
related diagnoses were PCP (19% [19] of 99 AIDS-related di-
agnoses), esophageal candidiasis (16% [16]), HIV wasting (15%
[15]), HIV dementia (12% [12]), and cytomegalovirus disease
(11% [11]). No difference in demographic characteristics by
sex was found, except that women were more likely to have
heterosexual contact as the HIV risk factor (67% [38 of 57]
among women vs. 40% [57 of 141] among men; *P* = .001).

The proportions of the 198 HIV-infected patients who had
documentation of specific health maintenance procedures are
shown in table 2. Among women, 53% had a mammogram
within 2 years of the most recent clinic visit, and 79% had a
Papanicolaou smear within 1 year. The majority of patients had
received pneumococcal vaccine within 5 years (86%), annual
Table 1. Demographic and clinical characteristics of 198 HIV-infected patients ≥55 years old.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median years (range)</td>
<td>59 (55–82)</td>
</tr>
<tr>
<td>Male sex</td>
<td>141 (71)</td>
</tr>
<tr>
<td>Race/ethnicity</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>98 (50)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>95 (48)</td>
</tr>
<tr>
<td>White, non-Hispanic</td>
<td>3 (1)</td>
</tr>
<tr>
<td>Asian</td>
<td>1 (1)</td>
</tr>
<tr>
<td>CD4+ cell count at initial visit, median cells/mm³ (range)</td>
<td>239 (0–1170)</td>
</tr>
<tr>
<td>AIDS diagnosis</td>
<td>132 (67)</td>
</tr>
<tr>
<td>By CD4+ cell count &lt;200 cells/mm³ only</td>
<td>56 (42)</td>
</tr>
<tr>
<td>With AIDS-defining clinical conditionsb</td>
<td>76 (58)</td>
</tr>
</tbody>
</table>

**NOTE.** Data are no. (%) of patients, unless otherwise indicated.

*A* At most recent clinic visit. 

*b* There were 99 conditions in 76 patients.

influenza vaccination (82%), annual tuberculin skin testing when indicated (77%), and serum cholesterol measurement at some time (68%). Formal evaluation of mental status at any time was documented for only 4% of patients. PCP prophylaxis was used when indicated for 96% of patients [15]. There were no differences among racial/ethnic groups in screening for cholesterol, tuberculin skin testing, formal mental status evaluation, provision of pneumococcal or influenza vaccination, performance of mammogram or Papanicolaou smears among women, or use of PCP prophylaxis. When health maintenance procedures among men and among women were compared, the only difference found was that, among eligible patients (excluding those who were allergic, who reported prior vaccination, or who refused vaccination), men (122 of 129) were more likely than women (45 of 53) to have received pneumococcal vaccination ($P = .04$).

For the subgroup of patients who received care after the introduction of HAART, 165 individuals seen after 1 July 1996, the demographic characteristics (age at most recent visit, race/ethnicity, and sex) were not significantly different from those of the other 33 patients. The median age at time of HIV diagnosis was 54 years (range, 43–75 years), and the median time of clinic follow-up was 29 months (range, 0–116 months). One hundred seven (65%) of these 165 patients had AIDS, and 58 (35%) had an AIDS-defining clinical condition.

Antiretroviral therapy was received by 140 (85%) of 165 patients at some point during follow-up: 11 (8%) of those patients received only NRTI monotherapy, 25 (18%) received dual NRTI therapy but not HAART, and 104 (74%) received HAART. Among the 104 patients who received HAART, 91 (88%) had a PI-containing regimen. Twenty-five (15%) of 165 patients were antiretroviral naive. Antiretroviral therapy was received by 95 (89%) of 107 patients with AIDS and by 45 (78%) of 58 patients without AIDS ($P = .06$). HAART was used significantly more often by patients with AIDS (75 [70%] of 107) than by those without (29 [50%] of 58) ($P = .01$). Receipt of HAART was not significantly related to sex, race/ethnicity, age group (55–64 vs. ≥65 years), HIV risk behavior, number of comorbid conditions, or number of concurrent HIV-unrelated drugs.

A total of 356 comorbid conditions were identified in 147 (89%) of 165 patients (95% CI, 84%–94%) (table 3). Among those with ≥1 comorbidity condition, the mean number was 2.4 conditions per person. A total of 363 medications for conditions other than HIV infection, HIV-associated opportunistic infections, or cancer were used for ≥6 months by 133 (81%) of 165 patients (95% CI, 74%–86%); the mean number of medications was 2.7 per person (table 3). Of the 133 patients with long-term use of HIV-unrelated medications, 112 (84%) also were receiving antiretroviral therapy (including 86 patients taking HAART) at the most recent clinic visit. The median number of concurrent HIV-unrelated medications was 2 (range, 1–6 medications) for patients receiving HAART and 3 (range, 1–9 medications) for those not receiving HAART ($P = .6$).

Thirty-eight (37%) of 104 patients using HAART discontinued antiretroviral therapy on ≥1 occasion because of toxicity; gastrointestinal intolerance, anemia, and rash were the most common side effects. Thirty-eight percent of patients (24 of 64) receiving ≥2 concurrent HIV-unrelated medications (the median number) discontinued HAART because of toxicity. The proportion among patients receiving <2 concurrent HIV-unrelated medications did not differ significantly (35%; 14 of 40) ($P =$

Table 2. Percentage of 198 HIV-infected patients ≥55 years old who had documentation of health maintenance procedures.

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Percentage of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumocystis carinii prophylaxis use</td>
<td>96</td>
</tr>
<tr>
<td>Measurement of serum cholesterol levels (any)</td>
<td>68</td>
</tr>
<tr>
<td>Annual tuberculin skin testing</td>
<td>77</td>
</tr>
<tr>
<td>Annual influenza vaccination</td>
<td>82</td>
</tr>
<tr>
<td>Pneumococcal vaccination every 5 years</td>
<td>86</td>
</tr>
<tr>
<td>Standardized mental status examination (any)</td>
<td>4</td>
</tr>
<tr>
<td>Mammogram (within 2 years)*</td>
<td>53</td>
</tr>
<tr>
<td>Annual Papanicolaou smear*</td>
<td>79</td>
</tr>
</tbody>
</table>

*a* Women only.
and 1 (14%) of 7 patients without a comorbid condition had a virus load <400 copies/mL (P = .23). Twenty-seven (40%) of 68 patients who received ≥1 concurrent HIV-unrelated medication and 5 (38%) of 13 who received no such medication had virus loads <400 copies/mL (P = .82). Thirty-six (24%) of 153 patients for whom such data were available had documentation of substance abuse. Neither use of HAART nor plasma HIV-1 load <400 copies/mL was significantly associated with substance abuse.

**DISCUSSION**

It is projected that by the year 2030, the number of individuals age ≥65 years will double, to >70 million, constituting 20% of the population of the United States [18]. The prevalence of HIV infection likely will increase as older individuals acquire new infections and the use of HAART leads to prolonged survival of individuals who were infected at a younger age. Management of disease in these patients will pose many challenges to our health care system. The results of this study of older HIV-infected individuals demonstrate the importance of heterosexual transmission of HIV, that the presence of comorbid conditions and long-term use of concurrent medications need not preclude the successful use of HAART, and that insufficient attention appears to have been given to cognitive screening.

Heterosexual transmission of HIV is growing in importance among older persons and accounts for 15% of AIDS cases in those >50 years old [2, 19–21]. However, older persons with HIV risk factors are less likely to have received HIV testing than are young adults [22]. Unsuspected HIV infection was identified (by testing discarded serum) in 5% of patients >60 years old who died in one New York City hospital [23].

In our study of HIV-infected inner-city residents ≥55 years old, heterosexual contact with a high-risk partner was identified as the major risk factor for HIV acquisition for almost one-half (47%) of the subjects, including 40% of male subjects. In comparison with a group of 7489 HIV-infected individuals with AIDS who were >50 years old in the United States in 1996 [2], our sample of individuals with AIDS (n = 132) had a higher proportion of women (29% in the present study vs. 16% in the larger group), Hispanic individuals (48% vs. 17%), injection drug users (30% vs. 19%), and individuals with risk from unprotected heterosexual behavior (46% vs. 15%) and had fewer white individuals (1% vs. 39%), MSM (7% vs. 36%), and individuals with no identified risk behavior (10% vs. 26%).

More than 80% of patients in our study had documentation of influenza and pneumococcal vaccination. Although it is not strictly comparable in terms of patient characteristics and is dependent on self-reporting, information on general use of these vaccines in New York State in 1997 is available from the Behavioral Risk Factor Surveillance System (BRFSS) [24–26].
Statewide, among persons ≥65 years old, influenza vaccination was reported among 65% and pneumococcal vaccination among 39%, with lower rates for persons of color (those who did not self-identify as white non-Hispanic) [26]. Therefore, the vaccination rates observed among our HIV-infected older patients compare quite favorably with rates reported among older individuals throughout New York State. This observation might reflect more frequent exposure to medical care among HIV-infected persons and heightened awareness of indications for vaccination recommendations by the HIV specialist or the patient. An unexpected finding was that women were less likely to have received pneumococcal vaccination than were men in our study, in contrast with national and statewide data, which did not demonstrate sex differences in this variable [25, 26]. It is important to study this further in HIV-infected persons of similar socioeconomic status.

In contrast, BRFSS data demonstrated that 78% of women in New York State aged ≥50 years reported having had a mammogram in the previous 2 years, yet only 53% of our sample of women had documentation of mammograms [24, 25]. It may be that less emphasis is placed on conditions unrelated to HIV disease by HIV specialists. This might explain the substantially lower rate of mammography among women in our study, compared with Papanicolaou smear screening, which was documented for 79% of our subjects. Unlike cervical neoplasia, which has been associated with HIV infection [27], no association between HIV infection and breast cancer has been established. However, it is important for clinicians to realize that HIV infection certainly does not protect against breast cancer, and therefore there is no rationale for relaxing surveillance for this important condition.

Documentation of any formal evaluation of cognitive function in our sample during the study period was rare. HIV-associated dementia has been reported in ~15% of HIV-infected adult patients, and older age at AIDS diagnosis is a significant risk factor [28, 29]. The impact of HIV-associated cognitive decline on psychosocial interactions, adherence to medications, and ability to benefit from educational intervention can be profound. Serial cognitive and neurologic evaluations have been recommended for the assessment and treatment of the neuropsychiatric aspects of AIDS [30]. Our study does not address the issue of whether lack of testing for cognitive decline reflects provider unawareness of the importance of HIV-associated dementia (formal cognitive function assessment was not required by any of the clinics during the study period) or the difficulty of performing formal tests in a clinic session.

More than one-third of individuals in the United States will have a chronic health-related condition that will affect their normal functioning by age 65 years [31]. Alterations in drug metabolism related to age and comorbid conditions may require dose adjustment or avoidance of certain medications or combinations of medications. The results of this study suggest that antiretroviral use by older patients need not be adversely affected by the presence of chronic comorbid conditions and polypharmacy associated with aging. Our findings indicate that discontinuation of HAART was not associated with concurrent use of other medications. Serious adverse reactions to medication occur more frequently among elderly individuals than among younger adults [18]. However, the proportion (37%) of HIV-infected patients ≥55 years old in our study who discontinued or modified HAART at least once because of toxicity is similar to that reported for adults of all ages [32].

Forty percent of the patients in our study who were receiving HAART at the time of their most recent recorded clinic visit had a concurrent plasma HIV-1 load <400 copies/mL. This is similar to reports from general clinical practice for HIV-infected patients of all ages, in which the rate of undetectable plasma HIV-1 load at ≥6 months after HAART initiation ranges from 37% to 44% [33–35]. The assumption that older individuals may have more difficulty in achieving success with complex antiretroviral therapy may be challenged by the absence of evidence in the present study that chronic medical conditions and long-term use of the drugs used to treat them were associated with inability to achieve undetectable virus loads.

It is of considerable concern that, after HAART became available, more than one-fourth of patients receiving treatment received suboptimal therapy. It seems possible that, despite the general availability of convincing data supporting its use, routine HAART was withheld by some clinicians at least until official guidelines were published, just 2 months before the end of our study period [17]. It will be important to determine whether prescription of HAART regardless of patient age has improved subsequently with increased familiarity of clinicians with official guidelines and increased experience using antiretroviral therapy.

Incomplete data availability and interobserver and institutional variation in documentation are limitations of a multi-institutional retrospective study. Observer bias was addressed to some extent by collecting data on the basis of strictly defined criteria and using standardized data-collection forms. Sample size was limited, and therefore the power for some analyses was not optimal.

Prospective studies are needed to determine virologic response and the rate and extent of immunologic recovery in older patients with HIV infection who are receiving HAART. Further studies also will be necessary to assess whether and how care delivered to older persons with HIV infection has changed as additional medications have become available and increasing numbers of patients have led to greater expertise on the part of many of the clinicians who provide their care.
References