Obesity among HIV Patients: The Latest Epidemic

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Abstract

Since the advent of HAART, studies have been conflicting regarding weight information among HIV patients. We performed a retrospective study among male HIV patients between June 2004 and June 2005 at two large Navy HIV clinics to describe the prevalence and factors associated with being overweight/obese. Rates of obesity/overweight among HIV positive patients were also compared to data from HIV-negative military personnel. Of the 661 HIV-infected patients, 419 (63%) were overweight/obese and only five (1%) were underweight. HIV patients had a mean age of 41.0 years (range 20-73 years) and were racially diverse. The prevalence rates of being overweight/obese at the last visit were similar among both HIV positive and negative military members. Being overweight/obese at the last clinic visit was associated with gaining weight during the course of HIV infection (10.4 vs. 4.0 lbs, p<0.001), hypertension (36% vs. 23%, p=0.001), low HDL (40% vs. 31%, p<0.001), and a higher CD4 cell count at last visit (592 vs. 499 cells/mm³, p<0.001). These data demonstrate that HIV patients in the HAART era are commonly overweight and/or obese with rates similar to the general population. Being overweight/obese is associated with hypertension and dyslipidemia. Weight assessment and management programs should be a part of routine HIV clinical care.

Keywords

HIV complications; obesity; antiretroviral therapy

Background

Although wasting was common early in the HIV epidemic, it has become less common with the advent of highly active antiretroviral therapy (HAART) [1,2]. With the exception of peripheral lipoatrophy linked to certain types of antiretroviral medications, there has been a restoration to health phenomenon leading to a decline in wasting and more obesity as HIV patients are living longer and gaining weight, similar to the general population [3,4]. A recent study in fact found that being overweight or obese are now more prevalent than wasting [5].
Although several studies have defined predictors for obesity/overweight among the general population, little data exist specifically among HIV patients [5]. The aim of this study was to describe the prevalence rates and factors associated with obesity among HIV patients at two large U.S. Navy HIV clinics.

Methods

We performed a retrospective study among all male HIV patients who underwent a visit at either the Naval Medical Center San Diego (NMCSD) or the National Naval Medical Center (NNMC) in Bethesda, Maryland between the dates of June 2004 and June 2005. Patients were military beneficiaries (active duty, retirees, or dependents) who were ≥18 years of age and had free access to medical care. All active male HIV patients were included in this study. Since the majority (>90%) of patients served in our clinic are male, we did not have adequate power to evaluate females; hence, we restricted the study to male patients. HIV positive status was verified prior to inclusion in the study. Of note, all military members are HIV-negative upon entry into military service and undergo routine screening for HIV during active duty service at intervals of approximately every two years. The study was approved by the Institutional Review Boards at both participating hospitals.

Data were collected by a review of the subjects’ medical/computerized health records. Data abstracted include baseline demographics, body mass index (BMI) at first clinic visit after HIV diagnosis and at last clinic visit, duration of HIV infection, medical conditions such as hypertension and diabetes, serum lipid levels, CD4 cell counts, and HIV viral loads. Antiretroviral (ARV) agents were captured at the last visit on all subjects, while duration of individual ARV agent use were available only for the NMCSD subjects. Since active duty members undergo mandatory weight monitoring programs biannually and are expected to maintain their weight within specified ‘normal’ ranges, which may influence their weights, we examined active duty status as a possible factor related to weight change in our study. These data on military status (active duty, retiree or dependent) were collected at one of the two study sites (NMCSD).

Weight was categorized using standardized definitions by the National Institutes of Health: a BMI <18.5 kg/m² as underweight; 18.5-24.9 kg/m² as normal weight; 25.0-29.9 kg/m² as overweight; and ≥30 kg/m² as obese [6]. Hypertension was defined as a clinical diagnosis with the use of an antihypertensive medication and/or blood pressures >140/90 mmHg on two of the three clinic visits. Diabetes was diagnosed as the use of an anti-diabetic medication and dyslipidemia as the presence of a total fasting cholesterol of >200 mg/dl, triglycerides>150 mg/dl, LDL>130 mg/dl, or an HDL <35 mg/dl. HAART was defined as two or more nucleoside reverse transcriptase inhibitors (NRTIs) in combination with at least one protease inhibitor (PI) or one non-nucleoside reverse transcriptase inhibitors (NNRTIs); one NRTI in combination with at least one PI and at least one NNRTI; or an abacavir or tenofovir containing regimen of three or more NRTIs.

Data among HIV-uninfected military members were collected from the annual report, “Department of Defense Survey of Health Related Behaviors among Active Duty Military Personnel” [7]. Data among naval male active duty members who were HIV-negative and with similar demographics were obtained from this report and served as a comparison group for HIV-positive male naval members in our study.

Statistical analyses included descriptive statistics with means reported as the data were normally distributed. Study outcomes included prevalence rates of obesity/overweight (categorized by BMI) at HIV diagnosis and at last study visit, as well as changes in weight (defined in terms of pounds) during the course of HIV infection. Analyses included evaluating...
factors associated with an elevated BMI at the last visit comparing HIV patients who were overweight/obese to patients who were underweight/normal weight at the last visit. In addition, we evaluated factors associated with weight gain during HIV infection. Univariate analyses utilizing Fishers exact testing and regression models depending if variables were categorical or continuous. Variables significant in the univariate models at a p<0.20 were included in backward stepwise logistic and linear regression models for categorical and continuous variables, respectively. Correlations testing between variables utilized Pearson correlation coefficients. A p-value <0.05 was considered statistically significant (STATA 9.0 software, StataCorp LP, College Station, TX).

Results

661 subjects satisfied the inclusion criteria. The mean age of the study population was 41.0 years (SD, 9.1; range 20-73 years) and race was reported as 50% Caucasian, 38% African American, 8% Hispanic, 3% Asian, and 1% other (Table 1). At their last visit, 8% of the study population was diabetic, 31% hypertensive, and 74% had dyslipidemia. The mean duration of HIV was 11 years (SD 5.8), mean CD4 count at the last visit was 558 cells/mm$^3$ (SD 282), and 73% of patients were receiving HAART. At the last clinic visit, 46% of our patients were overweight and 17% were obese. The mean BMI of our cohort at last visit was 26.6 (SD, 4.1). Comparing the weight of the patients at HIV diagnosis to their last visit (mean time of 9.6 years), there were significantly more HIV patients at the last visit who were overweight or obese than at the time of HIV diagnosis (63% vs. 54%, p<0.001 using a binomial probability test).

Over the course of HIV infection (mean 11 years), 72% gained weight (mean 9.7 lbs). Of the patients who were overweight or obese at their last visit, 80% gained weight during their HIV infection (mean 2.5 lbs/year) and 20% had lost weight (mean -1.4 lbs/year) or had no weight change. Of patients with a normal BMI at the most recent visit, 54% gained weight (mean 1.4 lbs/year) and 46% lost weight (-1.5 lbs/year) or had no change in weight. Only five (1%) patients were underweight at the last clinic visit.

We also evaluated our cohort for weight loss of >10% over the course of HIV infection; 24 patients (4.1%) had lost >10% of their weight based on measurements in pounds from the baseline to the last visit’s weight measurements. Of note, those who lost weight during the course of their HIV infection, the majority of these patients had a baseline BMI that was overweight/obese, whereas those who gained weight were more likely to be underweight or normal weight at HIV diagnosis (p<0.001).

Since our population consisted of military beneficiaries, we categorized a subset of our patient population who were from the San Diego clinical site (n=335) into those on military active duty service (n=137, 41%) and those who are retirees or dependents (n=198, 59%). Weight categories among active duty members and retirees/dependent were similar: 47% of active duty members were overweight compared to 49% of retirees/dependents; likewise, 17.5% of both active duty and retirees/dependents were obese. We then compared our data on HIV-infected active duty members to that of a representative population of HIV-negative male active duty members, we found no notable differences; the prevalence of being overweight among HIV negative personnel was 47.5% and obese was 18.4% [7]. Examining a BMI of <18.5 (i.e., underweight), 1% of HIV patients and 0.8% of HIV negative military members are in this category.

We examined the data for factors associated with an elevated BMI at the last visit by comparing HIV patients who were overweight/obese to those underweight/normal weight; univariate findings are shown in Table 1. HIV patients who were overweight/obese compared to those...
who were underweight/normal weight at the last visit were more likely to have gained weight during the course of HIV infection (10.4 vs. 4.0 lbs, p<0.001), have hypertension (36% vs. 23%, p=0.001), have hypertriglyceridemia (55% vs. 44%, p=0.005), have a low HDL (40% vs. 31%, p=0.03), less likely to have a CD4 cell nadir of <200 cells/mm³ (29% vs. 40%, p=0.006), and have a higher CD4 cell count at last visit (592 vs. 499 cells/mm³, p<0.001). Demographics (age and race), duration of HIV infection, follow-up time, HIV viral load, and antiretroviral therapy including protease inhibitors use were not significantly different. CD4 nadir and CD4 count at the last visit were both predictive in the univariate models and highly correlated (r=0.58, p<0.001). Likewise, hypertriglyceridemia and low HDL were also correlated (r=-0.24, p<0.001). Hence, variables included in the multivariate model were weight change, hypertension, low HDL level, and CD4 count at last visit; age, race and follow-up time were also initially included since they may affect weight. In the final multivariate model, being overweight/obese at the last visit was significantly associated with more weight gain over the course of the HIV infection (OR 1.03, p<0.001), higher CD4 cell count at last visit (OR 1.14 per 100 cells, p<0.001), low HDL level at last visit (OR 0.97, p<0.001), and diagnosis of hypertension (OR 1.95, p=0.001). The latter two findings are likely a result of being overweight or obese. The analysis for predictors of HIV patients’ weight at last visit was repeated using the last BMI as a continuous variable and the same associations were found.

We also examined the data for factors associated with weight gain during HIV infection. In the univariate linear regression analyses, weight gain was significantly associated with a younger age at HIV diagnosis (estimate -0.06, p<0.001), non-active duty status at last visit (0.76, p=0.02), higher LDL (0.01, p=0.03), longer duration of HIV infection (0.04, p=0.03), longer HAART use (0.01, p=0.01), and a longer follow-up time (0.08, p<0.001); there was a trend for higher CD4 cell counts at last visit (0.08, p=0.05). Weight gain during the course of HIV infection was also associated with having a lower baseline BMI (-0.14, p<0.001).

Duration of HIV and follow-up time were correlated, as were CD4 cell count, time on HAART, and duration of HIV. Duty status was not included due to the limited sample size of available data. Therefore, the multivariate model included age at HIV diagnosis, race, LDL, duration of HAART, last CD4 count, and time. The final multivariate model showed that weight gain during HIV infection was significantly related to younger age of HIV diagnosis and longer time of HIV follow-up. In addition, a higher CD4 cell count and higher LDL were associated with weight gain, with a trend for an association between hypertension and weight gain (p=0.07). HAART use was not predictive of weight gain in the final model.

**Discussion**

We found that 63% of HIV-infected patients in our study cohort are now overweight or obese, a higher rate than previously described among HIV patients [5]. These weight data are nearly identical to that of the U.S. general population [3] and a comparator HIV-negative military population [7]. These data suggest that during the HAART era, HIV patients are often overweight/obese similar to the general population. Of note, 54% of patients were already overweight or obese at the time of HIV diagnosis; this suggests that the incidence of becoming overweight/obese over the course of HIV infection may not be elevated compared to the general population.

Our study HIV cohort was unique since patients were diagnosed early in their HIV disease due mandatory HIV testing. Therefore, the weight gain noted in this study and the factors associated with excess weight in our cohort may be more consistent with that found in the general population and less related to HIV/AIDS or HAART effects.
Our data showed that an elevated BMI at last visit in the overweight or obese categories was associated with the diagnosis of hypertension and dyslipidemia, both of which are known risk factors for cardiovascular disease. Similar associations are well documented in the general population. These data suggest that screening and preventive measures for obesity among HIV-infected patients should be implemented within HIV clinics.

In addition, we noted that subjects with a CD4 nadir >200 cells/mm$^3$ had a higher BMI at the last clinic visit. This suggests that those who do not experience end-stage HIV disease are more likely to be overweight. This is in agreement with the literature regarding the relationship between end-stage AIDS and the development of wasting which was seen in the pre-HAART era [8]. Likewise, HIV patients who were overweight/obese, as well as those who gained weight during the course of their HIV infection, were more likely to have higher CD4 cell counts at the last visit. This may be related to the fact that those who do not experience end-stage disease or low CD4 cell counts are less likely to have wasting or unintentional weight loss. Some studies have suggested that HIV patients with higher BMIs may have slower rates of HIV progression and more robust CD4 cell counts [9-12], which could also account for the relationship seen in this study between BMI and CD4 cell counts, but this requires further investigation. Of note, a recent study examining the impact of BMI on the immunologic and virologic response to HAART showed no impact [13].

We also noted that younger age at HIV diagnosis was associated with more weight gain during follow-up visits. This finding remained after controlling for the possibility of differential follow-up time in our multivariate analyses between younger and older patients. These results may be related to the obesity epidemic among young persons within the U.S. due to consuming larger portions and the lack of exercise; however, our study did not evaluate diet or exercise.

We found no relationship between obesity and antiretroviral therapy. We specifically examined current receipt of HAART, months of HAART and PI use, and the current use of specific antiretroviral medications, and found no relationship with weight among our cohort. Regarding the association of HAART and weight gain, a cross-sectional study on obesity also found no association between weight and current ARV regimen [5]. Studies after the introduction of novel antiretroviral agents typically have demonstrated weight gain after medication introduction with a correlation between increased weight and successful virologic responses [14,15]. However, most of these studies have been of short duration and studies with longer follow-up times have often showed a peak, followed by a decline in weight [14-18]. Longer durations of antiretroviral therapy may actually result in development of lipoatrophy due to NRTI use and HIV itself which may lead to weight reduction. In addition, HAART may become less effective at controlling the virus over time due to the development of resistance. Hence, weight gain shortly after HAART initiation may be followed by weight reduction; more data are needed. To our knowledge, this is the first study on obesity to specifically examine the impact of duration of HAART use (mean use of 54 months) and its effect on weight change among HIV patients in a clinic-based setting.

Being underweight was uncommon in our study population with only 1% having a BMI of <18.5 kg/m$^2$. In order to more fully evaluate for the possibility of wasting in our cohort, we also evaluated for a 10% weight decline from baseline until last visit; although we did find that 4% of our HIV patients had lost 10% of their weight, most of these individuals were initially overweight. We did not collect data on whether the weight loss was intentional or not. Our findings contrast with the report by Wanke, et al which showed that 18% of patients loss >10% of their body weight since HIV diagnosis [19]. These differing results may be related to our population of early diagnosed HIV patients who had free and open access to medications, which differed from Wanke’s study population who had more advanced HIV disease.
Weight gain among HIV-infected persons may be a sign of the efficacy of HAART in reducing the occurrence of AIDS and wasting. As HIV patients live longer and the infection has been relegate to a chronic illness, patients with HIV may be now facing similar issues as the general population including excessive weight gain due to poor diet and exercise [20,21]. Some have suggested weight gain among HIV patients may also be related to their desire not to appear too thin, which could lead others to suspect their infection. Others have implicated potential poor self-esteem [5]. More data on the causes of excessive weight gain among HIV patients are needed.

Excessive weight has been associated with various adverse health outcomes including hypertension, diabetes, cancer, cardiovascular disease, and excess mortality among the general population [22-25]. Among HIV patients, an elevated BMI along with other ‘classic’ as well as ‘non-classic’ risk factors for atherosclerotic disease may put this group at particular risk for coronary events [26]. For example, recent studies have highlighted the risk of coronary disease among HIV patients including the potential link to inflammation associated with ongoing viral replication in the absence of HAART [27].

Although our study found significant predictors for elevated weights among HIV patients, the $R^2$ values for the final multivariate models were small (0.08). These data suggest that other factors beyond demographics or HIV-related factors, such as dietary and exercise habits, may be most important in determining the weight of HIV patients. Future studies should also consider collecting data on nutritional, social, and behavioral aspects of weight change among HIV patients.

This study had potential limitations. Although we did note associations between patient characteristics and weight gain, causation could not be established due to the study’s retrospective design. Furthermore, the study population consisted only of males, and risk factors for weight may be gender specific. The length of follow-up varied between participants, which may have led to underestimation of weight gain among those followed for shorter time periods; we did, however, adjust our analyses for the follow-up time. In addition, we only examined the patients’ first and last weights; interim weights could have provided more information on variables which may impact weight changes. Finally, we did not have information on body composition or changes in waist circumference.

In summary, two-thirds of HIV patients in our cohort are now overweight or obese, similar to the rate among HIV-negative persons demonstrating that the obesity epidemic now involves the HIV population. In contrast, being underweight or wasted was uncommon among HIV patients in our study population. Excess weight was associated with hypertension and dyslipidemia, both known risk factors for cardiovascular events. These data support the development of weight assessment and management programs as part of routine HIV clinical care.

References


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Table 1
Descriptive Characteristics and Univariate Analyses of HIV Patients by BMI at Last Visit Categorized as Overweight/Obese versus Underweight/Normal Weight

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total (n=661)</th>
<th>Underweight/NORMAL* (n=242)</th>
<th>Overweight/Obese* (n=419)</th>
<th>OR</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at last visit, years, mean (SD)</td>
<td>41.0 (9.1)</td>
<td>41.0 (10.1)</td>
<td>41.0 (8.5)</td>
<td>1.0</td>
<td>0.98</td>
</tr>
<tr>
<td>Ethnicity, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.09</td>
</tr>
<tr>
<td>Caucasian</td>
<td>329 (49.8%)</td>
<td>123 (50.8%)</td>
<td>206 (49.3%)</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>African-American</td>
<td>252 (38.2%)</td>
<td>94 (38.8%)</td>
<td>158 (37.8%)</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>57 (8.6%)</td>
<td>14 (5.8%)</td>
<td>43 (10.3%)</td>
<td>1.85</td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>17 (2.6%)</td>
<td>7 (2.9%)</td>
<td>10 (2.4%)</td>
<td>0.86</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>5 (0.8%)</td>
<td>4 (1.6%)</td>
<td>1 (0.2%)</td>
<td>0.15</td>
<td></td>
</tr>
<tr>
<td>Duty status ** n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Active Duty</td>
<td>137 (40.9%)</td>
<td>49 (42.6%)</td>
<td>88 (40.0%)</td>
<td>1.0</td>
<td>0.73</td>
</tr>
<tr>
<td>Retiree/Dependent</td>
<td>198 (59.1%)</td>
<td>66 (57.4%)</td>
<td>132 (60.0%)</td>
<td>1.10</td>
<td></td>
</tr>
<tr>
<td>Change in weight from HIV diagnosis to last visit, lbs, mean (SD)</td>
<td>7.7 (19.3)</td>
<td>4.0 (17.8)</td>
<td>10.4 (18.7)</td>
<td>1.03</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetes, n (%)</td>
<td>53 (8.0%)</td>
<td>19 (7.9%)</td>
<td>34 (8.1%)</td>
<td>1.05</td>
<td>1.0</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>207 (31.2%)</td>
<td>56 (23.0%)</td>
<td>151 (36.0%)</td>
<td>1.89</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Dyslipidemia at last visit ¥ n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Cholesterol &gt; 200 mg/dl</td>
<td>194 (30.3%)</td>
<td>82 (34.5%)</td>
<td>112 (27.9%)</td>
<td>0.74</td>
<td>0.09</td>
</tr>
<tr>
<td>Triglycerides &gt; 150 mg/dl</td>
<td>331 (50.8%)</td>
<td>105 (43.6%)</td>
<td>226 (55.1%)</td>
<td>1.59</td>
<td>0.005</td>
</tr>
<tr>
<td>Characteristic</td>
<td>Total (n=661)</td>
<td>Underweight/Normal* (n=242)</td>
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<tr>
<td>LDL&gt;130 mg/dl</td>
<td>136 (21.3%)</td>
<td>59 (24.8%)</td>
<td>77 (19.2%)</td>
<td>0.72</td>
<td>0.11</td>
</tr>
<tr>
<td>HDL&lt;35 mg/dl</td>
<td>240 (36.7%)</td>
<td>75 (31.1%)</td>
<td>165 (40.0%)</td>
<td>1.47</td>
<td>0.03</td>
</tr>
<tr>
<td>Duration of HIV, mean (SD)</td>
<td>11.1 (5.8)</td>
<td>11.4 (5.7)</td>
<td>10.9 (5.8)</td>
<td>0.98</td>
<td>0.28</td>
</tr>
<tr>
<td>Age at HIV diagnosis, years, mean (SD)</td>
<td>31.6 (7.9)</td>
<td>31.4 (8.6)</td>
<td>31.6 (7.5)</td>
<td>1.00</td>
<td>0.66</td>
</tr>
<tr>
<td>CD4 nadir &lt;200 (cells/mm$^3$), n (%)</td>
<td>215 (32.8%)</td>
<td>95 (39.8%)</td>
<td>120 (28.9%)</td>
<td>0.61</td>
<td>0.006</td>
</tr>
<tr>
<td>CD4 count at last visit(cells/mm$^3$), mean (SD)</td>
<td>557.7 (281.8)</td>
<td>499.2 (255.1)</td>
<td>592.0 (291.5)</td>
<td>1.13</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HIV viral load at last visit log$_{10}$ copies/ml, mean (SD)</td>
<td>2.7 (1.1)</td>
<td>2.6 (1.1)</td>
<td>2.7 (1.1)</td>
<td>1.04</td>
<td>0.60</td>
</tr>
<tr>
<td>Currently receiving HAART, y/n, n (%)</td>
<td>479 (72.5%)</td>
<td>184 (76.0%)</td>
<td>295 (70.4 %)</td>
<td>0.75</td>
<td>0.13</td>
</tr>
<tr>
<td>Currently receiving protease inhibitor, y/n **, n (%)</td>
<td>224 (68.1%)</td>
<td>77 (69.4%)</td>
<td>147 (67.4 %)</td>
<td>0.91</td>
<td>0.80</td>
</tr>
<tr>
<td>Duration of HAART, months **, mean (SD)</td>
<td>54.0 (40.6)</td>
<td>54.6 (40.8)</td>
<td>53.8 (40.7)</td>
<td>1.0</td>
<td>0.86</td>
</tr>
<tr>
<td>Duration of protease inhibitor, months **, mean (SD)</td>
<td>35.1 (35.5)</td>
<td>36.4 (35.3)</td>
<td>34.6 (35.8)</td>
<td>1.0</td>
<td>0.68</td>
</tr>
<tr>
<td>Follow-up time between baseline and current visits, years, mean (SD)</td>
<td>9.6 (10.1)</td>
<td>10.2 (10.2)</td>
<td>9.6 (8.4)</td>
<td>0.99</td>
<td>0.43</td>
</tr>
</tbody>
</table>

HAART, highly active antiretroviral therapy; HDL, high density lipoprotein; LDL, low density lipoprotein; n, number; SD, standard deviation.

Overall percentages in each category are expressed as percentage of total number for which data are available for given category and for BMI.

* Defined by BMI based on the NIH guidelines.

** Information solely from the clinic at NMCS&D.
Odds ratio calculated per 100 cells/mm$^3$ CD4 cells.

Presence of any lipid abnormality.