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Trend and causes of hospitalizations among patients with HIV entering care in Italy: a 15 years study from the ICONA cohort

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Background

Declining rates of hospitalizations for HIV+ occurred shortly after the availability of cART. These shifts were largely attributed to the effects of cART, which, by improving the immune status of HIV-infected persons, decreased the incidence of AIDS events.
However, trends in the late cART era are less defined, with some studies suggesting stabilization or increasing rates of hospitalization. This could be due to the occurrence of late presentation, aging of HIV population, development of chronic end-organ disease, toxicity from long-term ARV use, development of multidrug-resistant viruses.

Objectives

To evaluate the trend in hospitalizations rates occurred during 1997-2012 in persons with HIV entering specialized care in Italy.
To assess risk factors for hospitalizations.

Materials and Methods

Hospitalization data collection

The primary cause of hospitalization was grouped into 9 diagnostic categories; the main categories were:

- AIDS defining illness (ADI)
- Non-AIDS infections (e.g. pneumonia, endocarditis, meningitis,…)
- Liver/gastrointestinal diseases (e.g. chronic hepatitis, liver cirrhosis, pancreatitis, ESLD,…)
- Cardiovascular diseases (e.g. myocardial infraction, coronary hearth disease, cerebrovascular disease/stroke, heart failure,…)
- Non-AIDS cancer (e.g. primary lung cancer, HCC, breast cancer, …)

The remaining 4 categories included: renal, psychiatric, hematological and other diseases. Each hospitalization was placed into a single mutually exclusive category.

Study population

HIV-1-infected patients from the Icona Foundation Study enrolled during the period 1997-2012.

Inclusion criteria

A hospitalization was included if occurred at least 30 days after the enrollment and was defined as admission to any Italian hospital for two or more days, within 31/12/12.

Statistical Methods

Patients were followed-up from the baseline to a hospitalization or their last visit. Participants could be included in multiple periods and could contribute more than 1 hospitalization per period.

The incidence rate of hospitalizations was calculated as number of hospitalizations recorded after baseline divided by PYFU and expressed as rate per 100 PYFU, with 95% confidence intervals (CI).

The number of hospitalizations, PYFU, and rates of hospitalization (per 100 PYFU), due to all causes and within each diagnostic category, were calculated for individual study years, and the following a priori determined study periods, characterized by availability of different antiretrovirals: 1997-1999; 2000-2005; 2006-2009; 2010-2012.

These were defined as early cART (1997-1999: mainly non-boosted protease inhibitors-PI- and nevirapine), old generation cART (2000- 2005: first generation boosted PI-PI/r- and efavirenz), modern cART (2006-2009: second generation boosted PIs) and current cART (2010-2012: modern cART including in addition integrase inhibitors-INI and new non nucleosides-NNRTI).

Risk factors for hospitalization were assessed by univariable and multivariable Poisson regressions (using PYFU as the offset) by a generalized estimating equation (GEE) model with a sandwich covariance matrix estimator, to account for participants contributing multiple hospitalization events. Time dependent factors (i.e. age, CD4 count) were updated for each calendar year.

Results

Overall, during the study period 10,527 participants (25% females; 38% heterosexuals, 31% MSM, 23% IDU; 27% with HCV; median age 36 (IQR 31-429) for a total of 51,281 PYFU, were enrolled. Of these, 1,760 (17%) were hospitalized at least once in 3,094 separate hospital admissions (mean LOS 18±21days, corresponding to 0.27% of total PYFU). The most frequent diagnostic categories were ADI (37%), non-AIDS infections (19%), liver/gastrointestinal diseases (11%), non-AIDS cancers (6%) and cardiovascular diseases (4%).
The rate of hospitalization decreased from 17 in 1997 to 4 in 2012 (p<0.001, Fig. 1). Overall, a significant decrease by study period was observed in ADI (p<0.001), non AIDS infections (p<0.001) and liver/gastrointestinal (p<0.001) diagnostic categories; cardiovascular disease remained unchanged while for non-AIDS cancers a significant increase was observed (p<0.001, Fig. 2). Considering age, hospitalization for liver/gastrointestinal and cardiovascular diagnostic categories were more frequent among patients older than 50 years (Fig. 3).
In a multivariable Poisson model, older age, late presentation, IDU risk factor, a recent gap in care (defined as no visit at site study for at least 12 months) were associated with a significant increase of the risk of hospitalization, while higher CD4, more recent ART period and male gender were associated with a significant reduction of the risk of hospitalization (Table 1).

Figure 1

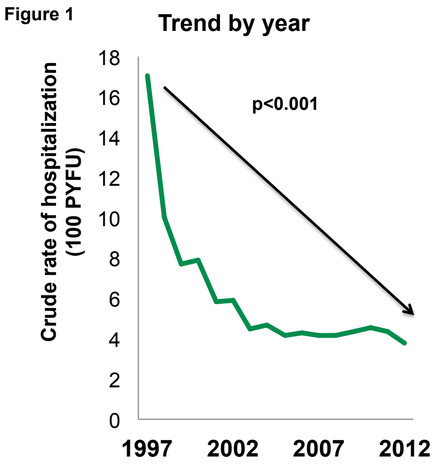


Figure 2

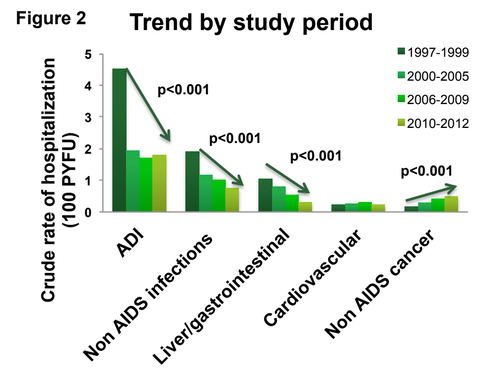
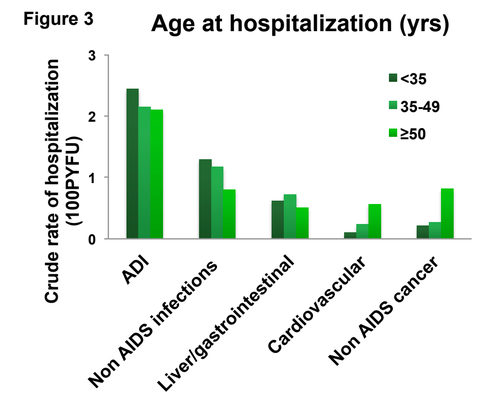


Figure 3



Poisson Regression		RR (95% CI)
Gender (ref F)	M	0.78** (0.72-0.86)
Age (ref 18-35)	36-49	0.99 (0.90-1.09)
	>=50	1.28** (1.13-1.45)
Late presentation (ref No)	Yes	1.13** (1.03-1.24)
Mode of transmission (ref IDU)	MSM	0.60** (0.52-0.68)
	HET	0.52** (0.47-0.59)
	Other/unk	0.85*(0.72-0.99)
Cd4 count (ref <200)	200-349	0.36** (0.32-0.40)
	350-499	0.21** (0.19-0.24)
	>=500	0.14** (0.12-0.15)
Recent gap in care (ref No)	Yes	2.19** (1.54-3.11)
ART period (ref 1997-1999)	2000-2005	0.79** (0.71-0.88)
	2006-2009	0.75** (0.67-0.85)
	2010-2012	0.73** (0.64-0.82)

**p<0.001

Conclusions

Hospitalization rates decreased during the period 1997-2012 in ICONA cohort especially in ADI, non AIDS infections and liver/gastrointestinal diagnostic categories; cardiovascular disease remained unchanged while for non-AIDS cancers a significant increase was observed. Considering age hospitalization for liver/gastrointestinal diseases and cardiovascular diseases were more frequent among patients older than 50 years.
These findings are related to a population of persons with HIV on care, and this may limit their generalizability to the overall population of persons living with HIV.

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