

Variazione del peso nelle persone sovrappeso e obese che vivono con HIV: l'impatto della pandemia da SARS-CoV-2.

Weight change in overweight and obese people living with HIV: the impact of SARS-CoV-2 pandemic.

Silvia Dettori^{1,2}, Sonia Lerta¹, Sabrina Bianchi¹, Federica Magnè², Sara Mora³, Mauro Giacomini³, Antonio Di Biagio^{1,2}, Matteo Bassetti^{1,2}, Lucia Taramasso²

¹ Department of Health Sciences (DISSAL), University of Genoa- Genoa, Italy

² Infectious Diseases Unit, Ospedale Policlinico San Martino IRCCS- Genoa, Italy

³ Department of Informatics Bioengineering, Robotics, and Systems Engineering (DIBRIS), University of Genoa- Genoa, Italy

Riassunto

La pandemia del virus SARS-CoV-2, iniziata in Italia a fine febbraio 2020, ha modificato le abitudini di vita, soprattutto durante il periodo di lockdown, causando una tendenza all'aumento di peso. Come nella popolazione generale, anche le persone che vivono con l'HIV (PWH) hanno mostrato un aumento del BMI negli ultimi anni e l'obesità è diventata un problema emergente. In questo studio abbiamo analizzato se il periodo della pandemia abbia influenzato l'aumento di peso (WG) nelle PWH sovrappeso e obese e quali fattori siano stati correlati al WG.

Durante il periodo pandemico, da marzo 2020 a gennaio 2022 (periodo 2), il WG è stato riscontrato in 196 (68%) PWH, mentre durante il periodo prepandemico, da gennaio 2010 a febbraio 2020 (periodo 1), il WG si era verificato in 230 (80%) PWH.

Il WG medio durante il periodo 2 è stato di +1.15 kg/anno (\pm deviazione standard 2.66): +1.27 (\pm 2.18) kg/anno nei PWH sovrappeso e +0.83 (\pm 3.67) kg/anno negli obesi, mentre il WG medio nel periodo 1 è stato +1.37 kg/anno (\pm 2.67): +1.11 (\pm 1.89) kg/anno nei soggetti sovrappeso e +2.12 (+4,05) kg/anno nei PWH obesi. Le persone obese hanno avuto un WG significativamente inferiore nel periodo 2 rispetto al periodo 1 ($p=0.028$), mentre tra i soggetti sovrappeso non è stata riscontrata alcuna differenza nei due periodi.

Il BMI ($p<0.001$) e l'obesità all'inizio del periodo 2 ($p=0.0055$), così come la circonferenza addominale ($p=0.003$) e la diagnosi di diabete ($p=0.017$) sono risultati inversamente correlati al WG durante la pandemia, mentre la durata dell'infezione da HIV è risultata correlata al WG in modo diretto ($p=0.0005$). Nessuna relazione è stata trovata tra il WG e il regime ART in corso.

Abstract

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) pandemic, started in Italy at the end of February 2020, changed life habits with lockdown measures, causing tendency in gaining weight. As in general population, also people living with HIV (PWH) showed increasing BMI in the past years and obesity became an emerging issue. In this study we analysed if the pandemic period influenced weight gain (WG) in overweight and obese PWH and which factors could be related to WG.

During the pre-pandemic period, from January 2010 to February 2020 (period 1), WG was found in 230 (80%) PWH, while during the pandemic period, from March 2020 to January 2022 (period 2), WG was found in 196 (68%) PWH.

Mean WG during period 1 was +1.37 (\pm standard deviation 2.67) kg/year, +1.11 (\pm 1.89) in overweight and +2.12 (\pm 4.05) kg/year in obese PWH, while in period 2 it was +1.15 kg/year (\pm 2.66), namely +1.27 (\pm 2.18) in overweight and +0.83 (\pm 3.67) kg/year in obese PWH. Obese PWH gained significantly less weight in period 2 than period 1 ($p=0.028$), while, among overweight PWH, no statistically significant difference was found between the two periods. BMI at the beginning of period 2 ($p<0.001$), as well as obesity ($p=0.0055$), abdominal circumference ($p=0.003$) and diabetes ($p=0.017$) were all inversely related to the extent of WG during the pandemic, while years of HIV infection were directly related to WG ($p=0.0005$). No relation was found between WG and the current ART regimen.

Corresponding author:

Silvia Dettori
Infectious Diseases Unit,
Department of Health
Sciences (DISSal)
University of Genoa,
Genoa, Italy
Via Pastore, 1- 16132
Genova, Italy
Phone:
0039 010 555 4667/4660

silvidetto@gmail.com

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Introduction

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) pandemic started in Italy at the end

of February 2020. The pandemic changed the lifestyle habits of many people, especially in the periods with lockdown measures, modifying daily

routine for work, ways of preparing and taking meals, often at home, sleep quality, especially in people who have reported depression or anxiety related to the global situation and personal issues, and possibility of outdoor and indoor sports activities (1,2). As a consequence and reaction to these issues, a certain part of the population had a tendency to gain weight during the pandemic, even defined as “covibesity” by some authors (3–5). This is in addition, in western countries, to the existing problem of obesity: global mean body mass index (BMI) increased globally of 0.4 kg/m²/decade for men and 0.5 for women from 1980 to 2008 (6). Data collected in Europe between 1997 and 2003 showed obesity prevalence between 6% and 20% with higher prevalence in Central and Eastern Europe (7) and in 2019, 52.7% of adult people were overweight (8). Obesity and overweight are related to comorbidities such as type 2 diabetes, cardiovascular diseases, stroke, obstructive sleep apnoea and premature death (9,10).

In the context of increasing prevalence of overweight and obesity, people living with HIV (PWH) are also involved (11). Different reasons were evaluated over time: longer life expectancy, and then age-related weight increase, better quality of life compared to the past, but also modern antiretroviral therapies (ART), in particular integrase inhibitors (INI) and tenofovir alafenamide (TAF) containing regimes, which have been associated with greater weight gain (WG) compared to older antiretrovirals (12–16). However, the impact of all these factors is poorly known on PWH diagnosed with obesity or overweight, and the additional burden of social and psychological factors related to the pandemic period is still poorly studied in this specific population.

The aim of this study was to evaluate if the pandemic period played a role in excessive WG in obese or overweight PWH followed up in a tertiary care University Hospital in Northern Italy. Secondary objective was to find factors related to WG during pandemic period.

Materials and Methods

This is a retrospective, single-centre observational cohort study conducted from January 2010 to January 2022 in a tertiary care hospital in Northern Italy. Study period was divided into two intervals: pre-pandemic period was considered from January

2010 to February 2020 (period 1) and the SARS-CoV-2 pandemic period was from March 2020 to January 2022 (period 2).

Data about overweight (BMI ≥ 25 and < 30 kg/m²) or obese (BMI ≥ 30 kg/m²) PWH were collected using an electronic data capture system called Ligurian HIV Clinical Network database (MEDINFO) (17). Information about sex, age, ethnic group, annual WG, current ART regimen, years of HIV infection, nadir CD4+, smoking, drug and alcohol abuse, comorbidities (diabetes, hypertension, metabolic syndrome, liver steatosis, psychiatric illness on treatment, stroke and myocardial infarction events), lipodystrophy, abdominal circumference measure were collected. Biochemical values of total (TC) and low-density lipoprotein (LDL) cholesterol, blood glucose and triglycerides (TG) were also analysed. Mean weight increase was compared in period 1 and period 2 through a paired t-test.

Factors associated to greater WG during period 2 were tested with a linear regression model in univariate and multivariable analysis. All variables with p value < 0.05 at univariate analysis were included in the multivariable model and tested by a stepwise procedure.

Results

A total of 288 PWH were enrolled in the study, 84 (29%) females, with mean age 54.4 (range 23–81) years and mean BMI at enrolment 29.5 kg/m². Among study participants, 193 (67%) were overweight and 95 (33%) obese at the time of enrolment in period 2. Among the latter group, 30 (32%) PWH became obese in the pandemic period. Descriptive study population data are shown in **Table 1**.

During period 2, WG was found in 196 (68%) PWH: 122 (63%) overweight and 74 (78%) obese. Mean WG during period 2 was +1.15 kg/year (± 2.66), +1.27 (± 2.18) kg/year in overweight and +0.83 (± 3.67) kg/year in obese PWH. Instead, during period 1, WG was found in 230 (80%) PWH: 145 (75%) overweight and 85 (89%) obese; the average WG was +1.37 kg/year (± 2.67): +1.11 (± 1.89) kg/year in overweight and +2.12 (± 4.05) kg/year in obese PWH. During period 2, obese PWH had significantly less WG compared to period 1 ($p=0.028$), while among overweight PWH no statistically difference in WG was found between the two periods (**Table 2**).

Table 1. Characteristics of study participants.

Participants n (%)	Total n=288 (100)	Overweight n=193 (67)	Obese n=95 (33)
Clinical characteristics			
Females n (%)	84 (29.1)	53 (27.4)	31 (32.6)
Mean age (± SD)	54.44 ± 9.85	54.44 ± 10.07	54.45 ± 9.43
Caucasian n (%)	235 (81.6)	152 (78.5)	83 (87.5)
HIV-RNA<50 copies/ml n (%)	275 (95.5)	186 (96.3)	89 (93.7)
Median CD4+ lymphocytes (IQR)	694.5 (480.5-902.7)	728 (486-929)	638.5 (435-822)
BMI 2021	29.42 ± 4.35	27.07 ± 1.42	34.2 ± 4.37
Weight 2021	86.2 ± 14.6	80.03 ± 9.49	98.83 ± 15.06
Mean weight change 2010-2021 (kg/years)	1.15 ± 1.64	0.79 ± 1.14	1.89 ± 2.17
Blood parameters of glucose and lipid metabolism			
Total cholesterol (2021)	192 ± 40	196 ± 40	185 ± 40
LDL-c (2021)	117 ± 34	119 ± 33	113 ± 35
HDL-c (2021)	51 ± 14	52 ± 15	50 ± 13
TC/HDL (2021)	3.96 ± 1.18	3.97 ± 1.15	3.96 ± 1.23
Triglycerides (2021)	138 (86-173)	135 (88.5-167)	144 (84-182)
Glycaemia* (2021)	104 ± 36	103 ± 39	105 ± 27
Lifestyle habits and comorbidities			
Current smoker	112 (38.9)	69 (35.7)	43 (45.3)
Former smoker	71 (24.6)	56 (29)	15 (15.8)
Current alcohol abuse	107 (37.1)	75 (38.9)	32 (33.7)
Former alcohol abuse	10 (3.5)	6 (3.1)	4 (4.2)
Current IDU	7 (2.4)	6 (3.1)	1 (1)
Former IDU	58 (20.1)	32 (16.6)	16 (16.8)
Diabetes	37 (12.8)	21 (10.9)	16 (16.8)
Hypertension	152 (52.7)	94 (48.7)	58 (61)
Metabolic syndrome	77 (26.7)	41 (21.2)	36 (37.9)
Fatty liver disease	98 (34)	61 (31.6)	37 (38.9)
Lipodystrophy	9 (3.1)	6 (3.1)	3 (3.1)
Stroke	6 (2)	2 (1)	4 (4.2)
Myocardial infarction	11 (3.8)	8 (4.1)	3 (2.9)
Psychiatric disorder	54 (18.7)	34 (17.6)	20 (21)
* Non-diabetic people BMI: body mass index; HDL: high-density lipoprotein; IDU: injection drugs users; LDL: low-density lipoprotein; TC: triglycerides			

Moreover, during period 2, 20 (20%) PWH with liver steatosis and 40 (52%) PWH with metabolic syndromes were newly diagnosed, but not statistically related to WG.

Four factors resulted inversely correlated with the amount of WG in course of period 2, at univariate analysis, namely BMI in 2019 (beta -0.287, 95% CI -0.381 – 0.193, $p < 0.0001$), abdominal circumference measurement (beta -0.081, 95% CI -0.134 – 0.028, $p = 0.0036$), being obese in 2019 (beta -1.451, 95% CI -2.402 – -0.500, $p = 0.003$) and

a previous diagnosis of diabetes (beta -1.882, 96% CI -3.136 – 0.628, $p = 0.0035$). On the contrary, TG increased more pronouncedly (beta 0.007, 95% CI 0.001 – 0.013, $p = 0.023$) in greater weight gainers, and years of HIV infection were also directly correlated to WG in period 2 (beta 0.084, 95% CI 0.043 – 0.125, $p = 0.0001$).

No significant relation was found among WG and other biochemical or viroimmunologic parameters, nor with lifestyle habits like current or former smoking or drug abuse, or with comorbidities like

Table 2. Comparison of weight gain prior and during SARS-CoV-2 pandemic period in overweight and obese people living with HIV.

Study population	Pre-pandemic period	SARS-COV-2 pandemic period	Delta WG Pandemic-pre-pandemic	95% CI	P value
All (N=288)	1.37 ± 2.67	1.15 ± 2.66	-0.22 ± 3.68	-0.65; 0.20	0.30
Overweight in 2019 (N=212)	1.11 ± 1.89	1.27 ± 2.18	0.16 ± 2.98	-0.24; 0.56	0.43
Obese in 2019 (N=76)	2.12 ± 4.05	0.83 ± 3.67	-1.29 ± 5.03	-2.44; -0.14	0.028

hypertension, lipodystrophy, psychiatric illness on treatment. No correlation was found between WG and the current ART regimen (data shown in **Table 3**). In multivariable model, BMI in 2019 (beta -0.256, 95% CI -0.352 – -0.160, $p < 0.001$), obesity in 2019 (beta -1.363, 95% CI -2.319 – -0.408, $p = 0.0055$), abdominal circumference (beta -0.086, 95% CI -0.142 – -0.030, $p = 0.003$) and previous diagnosis of diabetes (beta -1.538, 95% CI -2.797 – -0.278, $p = 0.017$) were confirmed to have a significant inverse correlation with WG in period 2. Also, length of HIV infection remained statistically related to WG (beta 0.075, 95% CI 0.033 – 0.117, $p = 0.0005$), as shown in **Table 3**.

Discussion

Considering the data emerged, we found a tendency to WG during the entire study period, both in overweight and obese PWH. These results confirmed the importance of WG issue in PWH and the possible metabolic implications derived. The WG described in most PWH in both study periods, is in line with the trend toward increasing BMI described in PWH in recent years (11,12). WG did not seem influenced by changes of life habits during the lockdown period in our study population. However, analysing the subgroups, an important difference emerged between obese and overweight people, with a greater WG among the second group in the pandemic period. Instead, obese PWH in 2019 gained significantly less weight in period 2 compared to period 1. Indeed, being obese in 2019 and people with diabetes or with a greater abdominal circumference were factors related to less WG during the pandemic period, suggesting that people at higher cardiometabolic risk might have been more aware and more sensitive to the problem of WG, and possibly more adherent to interventions to limit it during the study period, compared to overweight people. On the other hand, with lockdown measures, some people increased unhealthy behaviours like sedentary lifestyle, snacks consumption and cooking, and experienced also emotional changes like irritability, anxiety and sleep disturbances (1,2,18). These life changes might have influenced more overweight than obese PWH, perhaps because of some bad

behaviours among obese PWH also before the pandemic period.

As mentioned before, obesity is related to metabolic syndrome and cardiovascular diseases (10). Also, HIV infection is a condition that predisposes to diabetes mellitus and cardiovascular incidence events, as described by some authors (19–21). As a consequence, the tendency to WG could also be related with an increased risk of comorbidities. Educational interventions and lifestyle modifications are fundamental to improve PWH quality of life and to reduce comorbidities, as shown in several studies (22,23).

Intervention on diet and physical activity showed great results in improving control and reducing risk of diabetes and WG (24–26). So, educational strategies and health care follow-up could be fundamental in overweight PWH to avoid excessive WG and possible related comorbidities.

Even though WG has been associated in the past with longer life expectancy in HIV, nowadays it is also counted as a side effect of ART (13). In particular, regimens containing INI and TAF were the two most involved with registered increased weight in previous studies (27–29). Analysing our data, none of the ART regimens considered was related to WG during the pandemic period, even though it is a short period of time. Indeed, length of HIV infection was statistically related to WG ($p = 0.0005$) and this could be associated to the cumulative effect of drug exposure and people ageing, as also found in a previous studies (13).

The results of this study are limited by its retrospective design and the small sample size. Moreover, especially during early pandemic period, accessibility to outpatient service was reduced, so some weight changes could have not been captured. Despite those limitations, we found that the amount of yearly WG did not increase in overweight and obese people during the pandemic period, while obese PWH were even less likely to increase their body weight. Lockdown measures did not worsen the WG tendency in this specific population, in comparison to what observed in the general population. Educational strategies and health care follow-up are fundamental in PWH to avoid excessive increase in BMI and comorbidities

Table 3. Univariate and multivariable analysis of factors associated with greater weight gain in a cohort of overweight and obese people living with HIV during the SARS-CoV-2 pandemic period (difference between mean increase per year in the pandemic minus mean increase per year in the pre-pandemic period).

	Univariate				Multivariable			
	Beta	95% CI		p	Beta	95% CI		p
		lower	higher			lower	higher	
Sex	0.128	-0.809	1.065	0.79				
Ethnic group	-1.102	-2.290	0.086	0.07				
Age (by 1 year)	0.036	-0.007	0.079	0.11				
2010 BMI	-0.121	-0.284	0.042	0.14				
2019 BMI	-0.287	-0.381	-0.193	<0.0001	-0.256	-0.352	-0.160	<0.001
Obese in 2019 (BMI \geq30 kg/m²)	-1.451	-2.402	-0.500	0.003	-1.363	-2.319	-0.408	0.0055
Current smoker	0.788	-0.190	1.766	0.12				
Former smoker	-0.224	-1.324	0.876	0.69				
Current alcohol abuse	0.446	-0.446	1.338	0.33				
Current drug abuse	1.638	-1.131	4.407	0.25				
Lipodystrophy	-0.038	-2.484	2.408	0.97				
Diabetes	-1.882	-3.136	-0.628	0.0035	-1.538	-2.797	-0.278	0.017
Hypertension	-0.335	-1.188	0.518	0.44				
Metabolic syndrome	-0.607	-1.562	0.348	0.21				
New metabolic syndrome in period 2	-0.749	-2.011	0.513	0.25				
Steatosis	0.115	-0.847	1.077	0.81				
New steatosis in period 2	0.21	-1.393	1.813	0.8				
Psychiatric illness on treatment	-0.35	-1.459	0.759	0.53				
Abdominal circumference	-0.081	-0.134	-0.028	0.0036	-0.086	-0.142	-0.030	0.003
Current ART								
INI	-0.383	-1.238	0.472	0.38				
PI	0.422	-1.119	1.963	0.59				
NNRTI	0.33	-0.525	1.185	0.45				
TAF	0.816	-0.166	1.798	0.1				
TDF	0.725	-6.513	7.963	0.84				
Nadir CD4+	-0.226	-1.079	0.627	0.6				
Years HIV infection (by 1 year)	0.084	0.043	0.125	0.0001	0.075	0.033	0.117	0.0005
Glucose over time	0.003	-0.021	0.027	0.78				
Total cholesterol over time	0.007	-0.005	0.019	0.29				
Cholesterol LDL over time	0.005	-0.015	0.025	0.64				
Triglycerides over time	0.007	0.001	0.013	0.023	0.005	0.000	0.011	0.066

Multivariable models included all variables statistically significant at the univariate analysis. However, BMI 2019, obese 2019 and abdominal circumference were included in turn in the multivariable model.

* factors with $p < 0.05$ on univariate analysis were included in the multivariable model.

BMI: body mass index; **CI:** confidential interval; **HIV:** human immunodeficiency virus; **INI:** integrase inhibitors; **LDL:** low-density lipoprotein; **NNRTI:** non-nucleoside reverse transcriptase inhibitors; **PI:** protease inhibitors; **TAF:** tenofovir alafenamide; **TDF:** tenofovir disoproxil fumarate

development, to reach the “fourth 95” to better quality of life (30).

Conversely, no relation was found between WG and biochemical parameters analysed.

Moreover, although the current ART did not affect

WG during period 2, the duration of HIV infection did.

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