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COVID-19 hospitalization rates in individuals with substance or alcohol use disorders

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ARTICLE INFO

Keywords:

COVID-19

Hospitalisation

Mortality

Substance use disorder

Alcohol use disorder

ABSTRACT

People with Substance or Alcohol Use Disorders (SUDs/AUDs) are likely to be more vulnerable to COVID-19 infection than the general population.

We performed a cross-sectional study to compare the hospitalization rate (CHR) for COVID-19 in 2020 in patients diagnosed with SUDs or AUDs in the previous 10 years vs the population without these disorders (NAS). We included individuals who were resident in the Metropolitan Area of Bologna (Northern Italy).

People with SUDs or AUDs have a greater probability of being hospitalized for COVID-19 infection compared to the general population NAS, suggesting that they suffer from worse physical symptoms/conditions than the general population.

Furthermore, we found higher mortality rates during hospitalization for COVID-19 in patients with AUDs or SUDs than the general population NAS.

These findings highlight the importance of a careful monitoring and early intervention measures in these patients.

1. Introduction

People with Substance Use Disorders (SUDs) or Alcohol Use Disorders (AUDs) are likely to be more vulnerable to infectious disease and coronavirus (COVID-19) infection than the general population, due to specific behaviors associated to substance use, to the contexts in which these substances are taken or to the places where health care is provided, and to their physical (D'Ancona et al., 2021). From a recent meta-analysis, the presence of any substance use disorders was associated with an increased risk of COVID-19 mortality (OR 1.76 95% CI 1.27–2.44) (Vai et al., 2021).

Individuals diagnosed with SUDs have a complex clinical profile and unhealthy lifestyle that might result in an increased risk of COVID-19 and a worse prognosis (Benzano et al., 2021). In addition to pulmonary infections (Dubey et al., 2020), they are at higher risk for COVID-19 infection, and when they contract the disease, these patients have a higher risk of severe illness course, hospitalization and worse outcomes than other patients with COVID-19, due to a variety of biopsychosocial factors, and their unique social and health care needs (Melamed et al.,

2020; Wang et al., 2021). Risks are increased by the high level of physical and psychiatric comorbidity, use of drugs that impair the cardiovascular and respiratory systems, the social marginalization and the stigmatization that people who use drugs often experience (Baillargeon et al., 2021; EMCDDA, 2020a).

People with AUDs are at greater risk of contracting both viral and bacterial infections, including COVID-19 (Testino, 2020), and have significantly higher risk of developing COVID-19 compared to patients without AUDs (Wang et al., 2021). They are at greater risk of COVID-19 not only because of the impact of alcohol on their health but also because they are more likely to experience social marginality situations than other members of the population (WHO, 2020).

The pandemic may well increase the extent and severity of some addictive disorders. People with addictive disorders are particularly badly affected as a result of poverty, physical and mental health vulnerabilities and disruption of access to services (Marsden et al., 2020). Lockdown policies imposed by governments to decrease the spread of the virus in the population may represent a further risk factor for increasing alcohol consumption in people with AUDs, development of

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AUDs in at-risk individuals and relapse for those who were previously abstinent (Clay and Parker, 2020). Those who do relapse are at a high risk of harmful drinking and require a tailored approach for follow-up and intervention (Kim et al., 2020).

Based on the previous literature, this study tested the hypothesis that the hospitalization rate for COVID-19 and the mortality risk during hospitalization may be higher in individuals diagnosed with AUDs or SUDs compared to those with no-AUDs/SUDs (NAS), in a cohort of residents in the metropolitan area of Bologna (Northern Italy). We considered diagnoses of AUDs/SUDs received between 2009 and 2019, not just in the previous year as done previously (Baillargeon et al., 2021), and the hospitalization rate registered in the year 2020. The confirmation of our hypothesis would suggest the importance of a careful monitoring and early intervention measures in patients with AUDs or SUDs, to avoid or reduce the consequences of COVID-19 infection.

2. Methods

2.1. Health care services for alcohol and substance use disorders in Italy

In Italy, individuals with alcohol or substance use problems can seek treatment in territorial centers for addiction treatment (TATs), Community Mental Health Centers (MHs) or in Hospital wards (HAs). In these three different public health services, treatment is covered by the National Health Service; access is voluntary, through referral by general practitioner, by specialist or by other healthcare services and there are no specific inclusion/exclusion criteria.

The metropolitan area of Bologna is a densely-populated territory in the Emilia-Romagna region, situated in north-eastern Italy; it is made up of fifty municipalities spread across an area of around 3000 km² with a population of over 850,000 inhabitants; there are 10 Hospital, 9 TATs and 11 MHs.

2.2. Study design

We performed a cross-sectional study. We included all the residents in the metropolitan area of Bologna who were under care in a public health service (TAT, MH, HA) and were diagnosed for AUDs or SUDs between 2009 and 2019.

For this study, the data of patients aged 18/79 years and alive at 01/01/2020 were selected. Life status was verified at the registry offices of the municipality where the patients were living at the end of the study period or at death.

COVID-19 hospitalizations during 2020 in the metropolitan area of Bologna were identified using ICD9 Codes (V01.82 – Exposure to associated SARS-Coronavirus; 079.82 - associated SARS-Coronavirus infection; 480.3 - associated SARS-Coronavirus pneumonia) (Emilia-Romagna Region, 2020).

Records of COVID-19 hospitalization within the cohort of AUDs and SUDs were identified through cross-matching with EHR of patients discharged from the Hospitals in the Metropolitan Area of Bologna using a single anonymous identity code. Mortality was assessed directly from the EHR data.

2.3. Inclusion criteria

Data were collected from IT system of Local Health Unit of Bologna. Personal identifiers were used following the rules of privacy regulation.

Inclusion criteria were: (1) being resident in the Metropolitan Area of Bologna; (2) age \geq 18 years and \leq 79 years; (3) having received for the first time an ICD-9 (292, 304, 305.2–305.9, 977, 965.01, 965.02, 965.09, 969) or ICD-10 (f11-f19, x42) code of SUD in the period from 01/01/2009 to 31/12/2019, in any of National Health Services mentioned above; (4) having received for the first time an ICD-9 (291, 303, 305.0, 571.0–571.3, 357.5, 425.5, 980, 790.3, 977.3) or ICD-10

(f10, x45) code of AUD in the period from 01/01/2009 to 31/12/2019, in any of National Health Services mentioned above.

The study protocol was approved by the local research ethics committee (Cod. CE:20183).

2.4. Variables

For each participant we retrieved the following variables: age, sex, country of birth, residence, substances of abuse, contact sector, date of contact.

2.5. Statistical analyses

The resident population (18–79 years) in the metropolitan area of Bologna as of 01/01/2020 (Emilia-Romagna Region, 2021), separately by age and sex, was divided between (1) patients with AUDs, (2) patients with SUDs, (3) general population NAS.

Continuous and categorical variables were analyzed with Student's t and chi-squared test, respectively. Crude COVID-19 Hospitalization Rates (CHRs) per thousand residents were calculated. Among patients hospitalized for COVID-19, Crude Mortality Rates (CMRs) per thousand people hospitalized were calculated.

Using Poisson regression, the incidence rate ratios (IRRs) comparing (1) CHRs per 1000 residents and (2) CMRs per 1000 residents and relative 95% confidence intervals - between patients with AUDs or SUDs and NAS - were calculated, both unadjusted and adjusted, for sex and age.

A level of statistical significance of 0.05 two-tailed was considered. Stata 15.0 was used for the statistical analyses.

3. Results

3.1. Sample

During year 2020, in the Hospitals of the metropolitan area of Bologna 3420 residents aged 18–79 years were discharged with a COVID-19 diagnosis (40% females, 17.5% non-natives, mean age 61.1 Years), of which 324 (9.5%) died during hospitalization (33% females, 5.6% non-natives, mean age 71.6 years).

Among residents who were under care in a public health service (TAT, MH, HA) from 2009 to 2019, 8184 patients received the diagnosis of AUDs and 7043 patients received the diagnosis of SUDs. Among these, 5135 AUDs were aged 18/79 years and alive at 01/01/2020 (28.3% female, mean age 52.6 years, 21.4% non-natives; 77% first accessed to a TAT, 18.7% to a HA, 6.3% to a MH), and 6081 SUDs were aged 18/79 years and alive at 01/01/2020 (23.9% female, mean age 44.2 years, 16.4% non-natives; 50% heroin, 23% cocaine, 10% cannabis, 5% benzodiazepines, 5% opioids; 55.3% first accessed to a TAT, 37.1% to a HA, 7.6% to a MH).

3.2. COVID hospitalization in general population

Among general population, the CHR was 5.06 per 1000 residents, higher among males and increasing by age in both gender (Table 1).

Among the subjects hospitalized for COVID-19, the CMR was 94.74 per 1000 patients, higher for males and increasing by age (Table 2). Note that there were no deaths in the age-class 30/39 years among males and in patients aged less than 40 years among females.

3.3. COVID hospitalization in subjects with SUDs

Hospitalization - Out of 6081 SUD patients, 35 were discharged with a COVID-19 diagnosis and, compared to non-hospitalized patients (mean age 52.6 years), they had a higher average age (mean age 58.5 years, P 0.0007), but no statistically significant difference in terms of sex and native/non-native status were observed.

Table 1
COVID-19 Hospitalization Rates per 1000 residents.

	Population (676082 residents)						Alcohol use disorders (5135 residents)						Substance use disorders (6081 residents)					
	Total(3420 patientshospitalized)		Males(2053 patientshospitalized)		Females(1367 patientshospitalized)		Total(52 patientshospitalized)		Males(41 patientshospitalized)		Females(11 patientshospitalized)		Total(35 patientshospitalized)		Males(28 patientshospitalized)		Females(7 patientshospitalized)	
	CHR	95% CI	CHR	95% CI	CHR	95% CI	CHR	95% CI	CHR	95% CI	CHR	95% CI	CHR	95% CI	CHR	95% CI	CHR	95% CI
18/29 years	0.88	0.70-1.09	0.97	0.72-1.28	0.78	0.55-1.08	9.80	1.19-34.96	6.49	0.16-35.65	20.00	0.51-106.47	5.12	1.40-13.06	5.20	1.07-15.12	4.90	0.12-27.01
30/39 years	1.79	1.54-2.07	2.07	1.70-2.50	1.51	1.20-1.88	3.44	0.42-12.38	4.64	0.56-16.66	-	-	2.00	0.41-5.85	0.89	0.02-4.93	5.42	0.66-19.44
40/49 years	3.33	3.03-3.65	4.08	3.62-4.59	2.60	2.23-3.00	7.98	3.99-14.23	7.91	3.42-16.66	8.15	1.68-23.64	5.42	2.60-9.95	5.41	2.34-10.62	5.49	0.67-19.71
50/59 years	5.35	4.98-5.75	6.72	6.12-7.37	4.07	3.61-4.56	9.70	5.44-15.95	10.85	5.62-18.88	6.82	1.41-19.80	6.75	3.24-12.37	6.99	3.02-13.73	5.92	0.72-21.21
60/69 years	7.85	7.32-8.40	10.31	9.44-11.24	5.67	5.06-6.32	8.78	3.80-17.23	12.62	5.46-24.71	-	-	8.60	1.78-24.91	12.45	2.57-35.95	-	-
70/79 years	12.24	11.54-12.97	15.84	14.66-17.09	9.26	8.44-10.14	27.24	14.97-45.28	28.90	13.94-52.51	23.81	6.52-59.84	39.06	12.80-88.80	89.29	29.63-196.19	-	-
Total	5.06	4.89-5.23	6.23	5.97-6.51	3.94	3.74-4.16	10.13	7.57-13.26	11.14	8.00-15.08	7.57	3.79-13.51	5.76	4.01-8.00	6.05	4.03-8.74	4.81	1.94-9.89

Table 2
Crude mortality rates per 1000 patients hospitalized for COVID-19.

	Population (3420 hospitalizations)						Alcohol use disorders (52 hospitalizations)						Substance use disorders(35 hospitalizations)					
	Total (324 deaths)		Males (217 deaths)		Females (107 deaths)		Total (9 deaths)		Males (9 deaths)		Females (0 deaths)		Total (5 deaths)		Males (5 deaths)		Females (0 deaths)	
	CMR	95% CI	CMR	95% CI	CMR	95% CI	CMR	95% CI	CMR	95% CI	CMR	95% CI	CMR	95% CI	CMR	95% CI	CMR	95% CI
18/29 years	11.63	0.29-63.09	20.41	0.52-108.54	-	-	500.00	12.58-987.42	1000	25-1000	250.00	6.31-805.88	333.33	8.40-905.70	-	-	-	-
30/39 years	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
40/49 years	13.07	4.81-28.23	14.39	3.93-36.43	11.05	1.34-39.34	-	-	-	-	-	-	-	-	-	-	-	-
50/59 years	29.73	18.72-44.67	37.69	22.11-59.67	17.30	5.64-39.91	133.33	16.58-404.60	166.67	20.86-484.14	100.00	2.53-445.02	125.00	3.16-526.51	-	-	-	-
60/69 years	92.01	73.18-113.81	105.88	80.55-135.89	69.62	44.14-103.51	250.00	31.85-650.86	250.00	31.85-484.14	333.33	8.40-905.70	333.33	8.40-905.70	-	-	-	-
70/79 years	195.54	172.69-220	214.94	184.08-248.38	168.10	135.21-205.30	285.71	83.89-581.04	400.00	121.55-737.62	400.00	52.75-853.37	400.00	52.75-853.37	-	-	-	-
Total	94.74	85.13-105.05	105.70	92.73-119.81	78.27	64.59-93.80	173.08	82.33-303.28	219.51	105.61-376.14	142.86	48.06-302.57	178.57	60.64-368.93	-	-	-	-

Table 3
Poisson regression.

COVID-19 hospitalization								
	Substance Use Disorders				Alcohol Use Disorders			
	Unadjusted		Adjusted for sex and age		Unadjusted		Adjusted for sex and age	
	IRR	95% CI	IRR	95% CI	IRR	95% CI	IRR	95% CI
Males	0.97	0.67–1.42	1.41	0.97–2.06	1.79	1.32–2.44	1.68	1.23–2.28
Females	1.22	0.58–2.57	1.63	0.77–3.42	1.93	1.06–3.48	1.80	0.99–3.25
Total	1.14	0.82–1.60	1.44	1.03–2.01	2.01	1.53–2.65	1.70	1.29–2.24

Mortality during COVID-19 hospitalization								
	Substance Use Disorders				Alcohol Use Disorders			
	Unadjusted		Adjusted for age		Unadjusted		Adjusted for age	
	IRR	95% CI	IRR	95% CI	IRR	95% CI	IRR	95% CI
Males	1.70	0.70–4.14	2.78	1.14–6.76	2.12	1.09–4.14	2.58	1.33–5.04
Total	1.52	0.63–3.67	2.96	1.22–7.19	1.85	0.95–3.56	2.25	1.16–4.37

The CHR was 5.76 per 1000 residents, higher among males and increasing by age, with the exception of the 30/39 years age group, which records the lowest rate for males and the total. Note that there were no hospitalizations among females aged more than 59 years (Table 1).

In the multivariate analysis, the IRRs adjusted for sex and age (18/29 years, 30/39 years, 40/49 years, 50/59 years, 60/69 years, 70/79 years) were significantly higher for total SUD patients compared to the resident population NAS, while no statistically significant differences were observed when considering only females or males (Table 3).

Mortality - Among the subjects hospitalized for COVID-19, there were no deaths among females and patients aged between 30 and 49 years. The CMR was 142.86 per 1000 patients, higher for people aged more than 59 years (Table 2).

In the multivariate analysis, the IRRs adjusted for age (≤ 49 years, 50/59 years, 60/69 years, 70/79 years) were significantly higher for total and males SUD patients compared to the resident population NAS (Table 3).

3.4. COVID hospitalization in subjects with AUDs

Hospitalization - Out of 5135 AUD patients, 52 were discharged with a COVID-19 diagnosis and, compared to non-hospitalized patients (mean age 44.1 years), they had a higher average age (mean age 50.9 years, $P = 0.0007$), but no statistically significant difference in terms of sex and native/non-native status were observed.

The CHR was 10.13 per 1000 residents, higher for males and patients aged 70/79 years. Note that there were no hospitalizations in the 30/39 and 60/69 years age group among females.

In the multivariate analysis, the IRRs adjusted for sex and age (18/29 years, 30/39 years, 40/49 years, 50/59 years, 60/69 years, 70/79 years) were significantly higher for total and males AUD patients compared to the resident population NAS, while no statistically significant differences were observed when considering only females (Table 2).

Mortality - Among the subjects hospitalized for COVID-19, there were no deaths among females and patients aged between 30 and 49 years. The CMR was 173.08 per 1000 patients, higher for people aged between 18 and 29 years (Table 2).

In the multivariate analysis, the IRRs adjusted for age (≤ 49 years, 50/59 years, 60/69 years, 70/79 years) were significantly higher for total and males AUD patients compared to the resident population NAS (Table 3).

4. Discussion

Marginalized groups, particularly those with AUDs and SUDs, are more vulnerable to contract the COVID-19 infection and are also likely

to suffer from higher illness severity and greater psychosocial burden (Dubey et al., 2020).

There are many studies regarding the impact of the COVID-19 pandemic on substance and alcohol consumption (EMCDDA, 2020b; Rehm et al., 2020; Winstock et al., 2020), and previous evidence suggested an increased risk of becoming positive to COVID-19 in people with SUDs (Benzano et al., 2021) or AUDs (Testino, 2020). The COVID-19 pandemic has had considerable impact on alcohol use, with an increase in alcohol related emergencies, changes in alcohol use patterns, increased risk of contracting COVID-19, effect on alcohol policies and sales, and an effect on vulnerable groups (Murthy and Narasimha, 2021). Nonetheless, there are still few epidemiological studies comparing the prevalence of COVID-19 in patients with AUDs and/or SUDs to that of general population, supposedly NAS, particularly in terms of serious cases, such as those requiring hospital admission.

Our results supported the hypothesis that people with SUDs and/or AUDs have a greater probability of being hospitalized for COVID-19 infection and to die during hospitalization compared to the general population, suggesting that they suffer from worse physical symptoms/conditions than the general population. Indeed, in our study, based on a cohort of residents diagnosed with AUDs and/or SUDs from 2009 to 2019, the IRRs of hospitalization with a COVID-19 infection diagnosis and the IRRs of mortality during hospitalization were higher compared to the general population NAS.

People diagnosed with AUD or SUD showed elevated CHRs, higher for males, increasing by age among SUDs and more elevated for AUD patients aged 70/79 years. IRRs adjusted for sex and age were significantly higher both for AUD (1.70) and SUD (1.44) patients compared to the resident total population, confirming that these differences were not dependent from demographic variables.

Furthermore, we found higher rates of death during hospitalization for COVID-19 in male patients – no deaths among females - with AUDs and SUDs than the general population, higher for SUD patients aged more than 59 years and for AUD patients aged between 18 and 29 years. IRRs adjusted for age were significantly higher both for AUD (2.58) and SUD (2.78) male patients.

These data are partly confirmed by the results of previous studies, conducted at different times and with different methods, which showed a prevalence of SUDs ranging from 1.3% to 14.5% in patients hospitalized for COVID-19 (Hsu et al., 2020; Vallecillo et al., 2021). In particular, a greater risk of hospitalization and death was reported in people who were COVID-19 positives and had AUDs/SUDs compared to those without AUDs/SUDs (Baillargeon et al., 2021; Wang et al., 2021).

In conjunction with the previous literature, our findings underline the higher risk of negative health consequences in subjects with problematic substance consumption during the current pandemic. SUDs and AUDs should be considered a condition that increases the risk for

hospitalization related to COVID-19 and for mortality among patients hospitalized, perhaps partly as a consequence of the exacerbation of healthcare disparities, driven by socio-economic factors that place certain groups at increased risk both for AUDs/SUDs and adverse outcomes of COVID-19 infection (Wang et al., 2021).

The limitations of this study should be considered. First, our results were referred to a limited area of Northern Italy, and they may not be generalizable to other regions. The data used for the study were limited to demographic and structured diagnostic information collected through electronic health records, while further details such as socio-economic status and concomitant diseases were not available; on the other hand, the use of standard information and standard codification of diagnoses (ICD codes) implies that our results can be easily compared to other studies, and our approach can be easily applied to large sample sizes. Detailed clinical information concerning the severity of the AUDs/SUDs and the clinical course of COVID-19 infection during hospitalization (e. g., specific complications) were not available either.

5. Conclusions

This study confirmed the hypothesis that individuals with AUDs/SUDs have higher risk of symptomatic COVID-19 infection that requires hospitalization and of mortality among male patients hospitalized compared to the general population, with CHRs and adjusted IRRs higher in patients with AUDs or SUDs. This finding highlights the importance of a careful monitoring and early intervention measures in patients with AUDs or SUDs, to avoid or reduce the consequences of COVID-19 infection. Policies aiming at avoiding social marginalization and disparities in access to health care services may reduce the risk of poor prognosis of COVID-19 infection in patients with AUDs/SUDs.

Role of funding source

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration

None.

CRediT authorship contribution statement

Raimondo Maria Pavarin: Writing – review & editing. **Chiara Fabbrì:** Writing – review & editing. **Diana De Ronchi:** Writing – review & editing.

Declaration of Competing Interest

All authors declare that they have no conflicts of interest. We confirm that neither the manuscript nor any parts of its content are currently under consideration or published in another journal.

Acknowledgments

We are very grateful to Silvia Marani and Elsa Turino, Epidemiological Monitoring Center on Addictions, DSM-DP, AUSL, Bologna for their help in collecting data.

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