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Characteristics of the population with mild COVID-19 symptoms eligible for early treatment attended in a single center in Northern Italy



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ABSTRACT

After more than two years from the first COVID-19 detected case in Brescia, Northern Italy, monoclonal antibodies and antiviral therapy aimed at early treatment of mild COVID-19 in patients at risk of progression and of hospitalization has been approved in Italy. Here we report the characteristics of the population eligible for the COVID-19 early treatments at our COVID-19 Early Therapy Unit of the Infectious Diseases Department of the ASST Spedali Civili of Brescia, with the aim to evaluate the characteristics of the foreign and native groups. Up to March the 31st, 2022, a total of 559 patients were referred to our Unit for COVID-19 early treatment, where 7.6% were foreigners, a group significantly younger than natives ($p < 0.05$). Particular differences are noticed between the native and the foreign population, where people aged > 65 years old were significantly more frequent among italians (39.7% vs 16.3%, $p < 0.01$), while primary or acquired immunodeficiencies were more frequent in foreigners (55.8% vs 38.9%, $p = 0.03$). Substantial differences are noted between native and foreign populations, where 14% and 26% ($p < 0.05$) respectively have never been vaccinated for COVID-19. Overall, 71% of the referred patients received an early treatment for mild COVID-19, with no differences between the two groups. Overall, on day 28 after treatment, 23 (4%) patients had been hospitalized due to COVID-19 related complications and four died (0.7%), no one was foreigner. In conclusion, while the treatment offered for mild COVID-19 appears to be rather uniform between the native and the foreign populations, some differences, especially in preventive vaccination COVID-19, must be taken into account.

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1. Introduction

At the beginning of the pandemic, Italy was the European COVID-19 epicenter, and the province of Brescia, Northern Italy, was one of the first and most affected Western areas.

After more than two years from the first detected case, some treatments are proved effective against SARS-CoV-2 whether initiated in the early phase of the disease in people with mild/moderate symptoms who also have other health conditions increasing their likelihood of developing progressive COVID-19 related disease [1].

Monoclonal antibodies therapy aimed at early treatment of mild/moderate COVID-19 in patients at risk of progression and of

hospitalization has been approved in Italy since June 2021, while antiviral drugs (ritonavir-boosted nirmatrelvir and molnupinavir) for the same purpose were released at the beginning of 2022 [1].

Based on the impossibility to offer these therapies to all SARS-CoV-2 infected non-hospitalized patients, health authorities have recommend to prioritize the treatment of patients who are at the highest risk of clinical progression according to: age, vaccination status, immune status, and the presence of risk factors, including obesity, diabetes and severe cardiological/neurological or lung disease.

Brescia has always been characterized by being one of the Italian provinces with the highest presence of foreigners in its territory, which, in 2021, reached 12.4% of the resident population [2]. Many studies have shown that the COVID-19 pandemic has disproportionately impacted the foreign population, especially forced migrants living in high-resource countries [3]. Substantial differences in the management of SARS-CoV-2 infection were also found

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Table 1
Characteristics of the population with mild SARS-CoV-2 infection referred for COVID-19 early treatment.

	TOTAL n (%)	NATIVES n (%)	FOREIGNERS n (%)
Referred population	559	516 (92.3%)	43 (7.6%)
Sex (Female)	263 (47%)	239 (46.3%)	24 (55.8%)
Age (median)	63.3	65.2	49.6
RISK FACTORS			
Immunodeficiency	225 (40.2%)	201 (38.9%)	24 (55.8%)
Age over 65 years old	212 (37.9%)	205 (39.7%)	7 (16.3%)
Cardio cerebral-vascular disease	196 (35%)	185 (35.8%)	11 (25.5%)
BMI > 30	102 (18.2%)	102 (19.7%)	0
COPD	85 (15.2%)	81 (15.7%)	4 (9.3%)
Chronic kidney disease	73 (13%)	64 (12.4%)	9 (21%)
Diabetes	42 (7.5%)	38 (7.3%)	4 (9.3%)
Cancer pathology	71 (12.7%)	69 (13.3%)	2 (4.6%)
Hematological diseases	23 (4%)	22 (4.2%)	1 (2.3%)
Neurodevelopmental and neurodegenerative diseases	13 (2.3%)	13 (2.5%)	0
Transplant	21 (3.7%)	19 (3.6%)	2 (4.6%)
Chronic liver disease	22 (3.9%)	18 (3.4%)	4 (9.3%)
Haemoglobinopathies	6 (1%)	5 (1%)	1 (2.3%)
COVID-19 VACCINATION COVERAGE			
Unvaccinated (0 doses)	85 (15%)	74 (14%)	11 (26%)
Completely vaccinated (3 doses)	282 (50.4%)	268 (52%)	14 (33%)
EARLY TREATMENT			
Early treatment received	397 (71%)	367 (71%)	30 (69.7%)
Monoclonal antibodies	257 (64.7%)	237 (64.5%)	20 (66.6%)
Antiviral	140 (35.2%)	130 (35.4%)	10 (33.3%)
COVID-19 OUTCOME			
Hospitalization due to COVID-19	23 (4%)	23 (4.4%)	0
Death	4 (0.7%)	4 (0.7%)	0

*COPD=Chronic obstructive pulmonary disease;

BMI=Body mass index

in the foreign population in Italy, who had lower vaccination rates and less access to diagnostic tests than the native population [4].

Here we report the characteristics of the population eligible for the COVID-19 early treatments at our COVID-19 Early Therapy Unit of the Infectious Diseases Department of the ASST Spedali Civili of Brescia. Aim of this study is to evaluate the characteristics of the foreign and native population eligible for the COVID-19 early treatment.

2. Methods

We performed an observational, retrospective, monocentric study. Patients were referred to our center after a diagnosis of COVID-19 performed by the General Practitioner or by another Specialist through a nasal swab for the research of SARS-CoV-2.

We included in our study all patients with mild COVID-19 symptoms eligible for COVID-19 early treatment according to the indications provided by Agenzia Italiana del Farmaco (AIFA) from the 22nd of aprile, 2021 up to the 31st of march 2022 [4]. Eligible patients aged 18 years or older and tested positive for SARS-CoV-2 with mild symptom onset within the prior 7 days were included. Mild COVID-19 illness is defined by mild symptoms (fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhea, loss of taste and smell) without dyspnea or abnormal chest imaging. In our center, patients with moderate COVID-19 - defined by the presence of clinical or radiographic evidence of lower respiratory tract infection with oxygen saturations that exceed 94% - were hospitalized, therefore they were not included in this study. [5].

They had at least one risk factor for COVID-19 progression among the following: age 65 years or older, diabetes requiring medication, obesity (body mass index > 30), chronic kidney disease, chronic liver disease, cardiological disease, bronchopneumopathy (chronic obstructive pulmonary disease or severe asthma), solid organ or hematopoietic stem cell transplant, hematological disease, oncological disease or other immunodeficiencies. Patients were excluded if they were hospitalized for COVID-19 pneumonia or if they had signs or symptoms of severe COVID-19.

Epidemiological, clinical and therapeutic data were retrieved from clinical charts. Results are reported as prevalences. Chi-squared test was used to compare results between the Italian and foreign population, where differences were considered significant when $p < 0.05$ (Epi Info 7.2 software).

The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Ethics Committee of Hospital (reference code NP-5363 approved on 26/04/2022).

3. Results

Up to March the 31st, 2022, a total of 559 patients were referred to our Unit for COVID-19 early treatment, where 7.6% were foreigners ($n = 43$). The great majority of foreigners were from the WHO European Region (60.4%; $n = 26$), all of which from Eastern European countries. Six patients were from the African Region (14%), 4 from the South-East Asian Region (9%), three patients were from the Americas (7%) and three from Eastern Mediterranean Region (7%), while only one was from the Western Pacific Region (2%).

The great majority (60.4%) were from the WHO European Region, all of which from Eastern European countries, and 14% and 9% were from the WHO African and South-East Asian Region respectively.

The proportion of female patients was 47%, with a similar balance both in Italians and foreigners (46% and 56% respectively). Median age was 63.3 in the overall population with significant differences in foreigners compared to natives (49.6 vs 65.2 years old, respectively, $p < 0.01$).

Concerning the risk factor for COVID-19 progression, the referred population presented: primary or acquired immunodeficiency (40%); age over 65 years old (38%); cardio cerebral-vascular disease (35%); BMI > 30 (18%); COBP (15%); chronic kidney disease (13%); diabetes (7.5%); cancer pathology (13%); hematological diseases (4%); transplant (4%), chronic liver disease (4%) and haemoglobinopathies (1%). Particular differences are noticed between the native and the foreign population, where people aged > 65 years old were significantly more frequent among italians (39.7% vs 16.3%, $p < 0.01$), while

primary or acquired immunodeficiencies were more frequent in foreigners (55.8% vs 38.9%, $p = 0.03$) (Table 1).

Half of the referred population (50.4%) had received the full three-dose COVID-19 vaccination cycle, while 27.7% had received two doses and 15% had not received any. Substantial differences are noted between native and foreign populations, where 14% and 26% ($p < 0.05$) respectively have never been vaccinated for COVID-19. Even among those who have completed the vaccination cycle with three doses there are significant differences between the two populations (52% in Italians and 33% in foreigners, $p < 0.05$).

Overall, 71% ($N = 397$) of the referred patients received the early treatment for mild COVID-19, with no differences between the two groups (69% in the foreigners, 71% in native patients). In particular, 65% received monoclonal antibodies and 35% received antivirals. More specifically, for those treated with monoclonal, 50% received sotrovimab, 36.7% banlanivimab-etesevimab and 13% casirivimab; molnupinavir (40.7%), ritonavir-boosted nirmatrelvir (34.2%) and remdesivir (25%) were the antivirals administered.

Those who did not receive any treatments, either refused ($N = 63$; 38.8%), had exceeded the limit of days from infection ($N = 15$; 9.2%) or did not meet criteria for the therapy (asymptomatic or hospitalized) ($n = 73$; 45%). We did not find differences between the proportion of foreigners and natives who did not receive treatment (30% in foreigners and 29% in Italians).

Overall, on day 28 after treatment, 23 (4%) patients had been hospitalized due to COVID-19 related complications and four died (0.7%), no one was foreigner.

4. Discussion

In this study we did not find any significant differences in either treatment rates or type of early treatment between foreigners and natives patients with mild COVID-19.

However, the two populations differ for some demographics and clinical risk factors, such as younger age and higher rate of immunodeficiencies among foreigners, who were also significantly less vaccinated for COVID-19 ($p < 0.05$).

The percentage of foreign patients who acceded to early treatment for COVID-19 in our study (8%) is slightly lower than the proportion of foreign people resident in our territory (12%) [4] (data not shown).

This difference may reflect the fact that the migrant population is often younger), and then, supposedly healthier, in comparison with the native one [4]. Another reason for this difference may be also partly attributed to the existing barriers in the access to health care services, whether due to language, document situation or cultural gap, in the foreign population [3]. Moreover, challenges in the fruition of the health care services have been exacerbated by the COVID-19 pandemic, and this may have reduced the access to health services in the non-Italian population [6].

Interestingly, either primary or secondary immunodeficiency were the first criteria for eligibility to early treatment for COVID-19 in migrants, showing that a vast part of the migrant population

referred to our Unit was composed by foreign patients that were already followed in other Departments for chronic diseases and therefore already chronically linked to the National Health Care System. Despite this, foreigners showed significantly lower rates of COVID-19 vaccination ($p < 0.05$) in comparison to Italians. These results are in accordance with our recent population-based study that included all residents in our province where 25.3% of foreign people had not received any vaccination dose, against 8.7% of the Italian population at the end of the 2021 [4]. We believe that this data should be carefully taken into account by the policy makers, as long as it proves, once again, that this population is scarcely tailored by the public health message. Our data on follow-up showing no death and no COVID-19-related hospitalization in the foreign group are probably due to the younger age of this population.

This is the first study describing characteristics of patients with mild COVID-19 symptoms, with a particular focus on geographic origin. However our study has several limitations. First of all, the retrospective nature, the monocentric design and the modest size of the study group do not consent to extend these findings to other settings. Moreover, we analyzed the foreign group without distinctions in document situation, geographical origin and duration of stay in Italy, which are some of the most important factors that determine the possibility of access to health services.

In conclusion, while the treatment offered for mild COVID-19 appears to be rather uniform between the native and the foreign populations, some differences, especially in preventive measures, must be taken into account in order to implement ad hoc tailored strategies for the two populations.

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