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Community use of antibiotics during the COVID-19 lockdown

To the Editor,

Within the ongoing COVID-19 pandemic, the occurrence of respiratory tract infection caused by other agents is of interest. In a recent report from China in this journal, patients of a fever clinic, including suspected cases of COVID-19 with fever and cough, were tested for the presence of SARS-CoV-2, influenza A, influenza B, adenovirus and respiratory syncytial virus [1]. Among 27,433 cases, only 42 (0.15%) patients showed evidence of any of these viral infections. The authors suggested that strict personal protection measures might contribute to such a low incidence of respiratory virus infection. Given the impact on the circulation of infections, the COVID-19 lockdown could have changed the panorama of community-acquired infections, with subsequent effects also on the total consumption of antibiotics. Here azithromycin may have a special place as, in the early stages of the pandemic, some literature data, not subsequently confirmed, suggested its activity against COVID-19 when combined with hydroxychloroquine [2–4].

Our study aims to assess whether the COVID-19 lockdown has had an impact on the use of systemic antibiotics in the community in the Emilia-Romagna region (Italy) by comparing consumption of March, April and May 2020 with the same months of the previous two years. The secondary objective is to provide details on azithromycin consumption.

The study was based on the regional drug database of outpatient prescriptions reimbursed by the Regional Health Service in Emilia Romagna, a northern Italian region of 4.5 million inhabitants. Antibiotics were classified according to the Anatomical Therapeutic Chemical (ATC) classification system of the World Health Organization and the use was measured in Defined Daily Dose (DDD) [5]. Consumptions in the general population were calculated as DDD per 1000 inhabitants

per day for antibacterials for systemic use (ATC J01) and of azithromycin (ATC J01FA10). Percentage distribution of antibiotic consumption in the general population was provided by class categorized as: penicillins with extended spectrum (J01CA); combinations of penicillins, including beta-lactamase inhibitors (ATC J01CR); macrolides (ATC J01FA); fluoroquinolones (ATC J01MA); cephalosporins (ATC J01DB; J01DC; J01DD; J01DE); others (all other ATC J01). For children 0–13 years, the prescription rate (prescriptions per 1000 children per month) of antibacterials for systemic use (ATC J01) was provided. Comparison of consumption was performed by month and year in the period March–May 2018, 2019 and 2020. STATA version 14.2 (Stata Statistical Software: Release 14, 2015, StataCorp LP, College Station, TX) was used for the analysis. Poisson regression was performed to evaluate rate changes. A significance level of .05 was considered in the analysis.

Consumption rates of antibacterials for systemic use (ATC J01) in the general population were 11.8, 7.3 and 6.4 DDD per 1000 inhabitants per day, in March, April and May 2020 respectively, with a variation of –22%, –44% and –53%, compared to the average rates registered in the same months in 2018–2019 (Figure 1). All the observed variations were highly significant ($p < .001$). The aggregate consumption rates for the third quarter (July–September) of 2018 and 2019 had been 10.5 DDD per 1000 inhabitants per day.

Considering the percentage distribution on antibiotic consumption of the March–May period, combinations of penicillins, including beta-lactamase inhibitors were the most prescribed category (36% in 2020 vs. 37% in 2018–2019) followed by macrolides (24% in 2020 vs. 21% in 2018–2019), fluoroquinolones (10% in 2020 vs 11% in 2018–2019), cephalosporins (10% in 2020 vs 11% in 2018–2019) and penicillins with extended spectrum (9% in 2020 vs 13% in 2018–2019); other agents

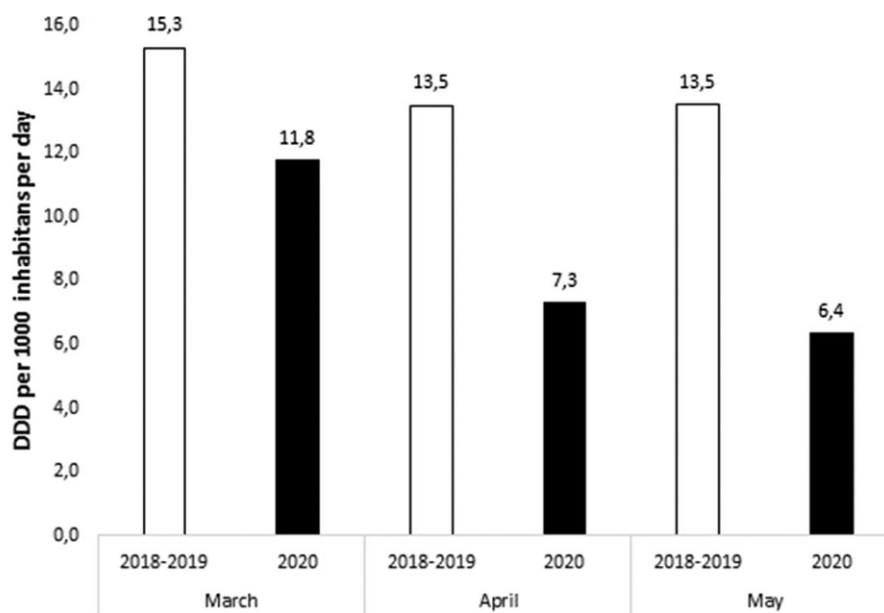


Figure 1. Community consumption of systemic antibiotics (J01) in Emilia-Romagna Region: comparison by month and year (period March–May 2018–2019 and 2020).

accounted for 11% and 8% of all antibacterial consumption in 2020 and 2018–2019, respectively.

Consumption rates of azithromycin (ATC J01FA10) in March, April and May 2020 were 1.8, 1.2 and 0.6 DDD per 1000 inhabitants per day, respectively, with a variation of +23%, –2% and –48%, compared to the averages registered in the same months in 2018–2019. In March 2020, azithromycin was prescribed in combination with hydroxychloroquine or chloroquine in 2.1% of cases and in combination with other antibacterials (mainly penicillins or cephalosporins) in 14.4% of cases. In contrast, in March 2018–2019, azithromycin was prescribed in combination with hydroxychloroquine or chloroquine and with other antibacterials in 0.1% and 6.3% of cases, respectively.

Prescription rates of antibacterials for systemic use (ATC J01) in the population 0–13 years were 325.7, 156.1 and 120.5 prescriptions per 1000 children per month, respectively in March, April and May 2020, with a variation of –67%, –81% and –85%, compared to the average rates registered in the same months of 2018–2019.

The study results show that the lockdown influenced the antibiotic prescriptions at the community level in Emilia-Romagna Region. In fact, in March and April 2020, there was a relevant reduction in antibiotic consumption which also continued in May; this was more evident in children as day-care centres and schools had been closed since the last week of February 2020. Comparing the period March–May of 2020 and 2018–2019, the percentage distribution of the categories of antibiotics did not change importantly, except for a relative increase in

the use of macrolides and a decrease in the use of penicillins with extended spectrum. Overall consumption rates in 2020 were comparable or lower than summer average of the previous two years. Instead, the use of azithromycin increased significantly before the Italian Medicines Agency had recommended, on 9 April 2020, not to use this antibiotic, alone or in combination with other drugs, for the treatment of COVID-19 except in the case of bacterial infections [6]. This finding is likely related to a therapeutic approach, based on insufficient evidence, suggesting a potential efficacy of azithromycin against COVID-19 when combined with hydroxychloroquine [2–4]. It should also be noted that, although azithromycin was widely used during the first phase of the pandemic, in the vast majority of cases it was not prescribed in combination with hydroxychloroquine or chloroquine. Moreover, this antibiotic was more frequently prescribed in combination with other antibacterials in March 2020 compared with the same month of 2018–2019 (14% vs. 6%); this finding could suggest that azithromycin has been used, at least in some cases, in combination with other antibiotics (i.e. penicillins or cephalosporins) for the treatment of community-acquired pneumonia in patients with suspected COVID-19 infection.

The reduction in overall antibiotic consumption suggests that the lockdown, which led to the control of COVID-19, also had a significant impact on the transmission dynamics of other infections. It is also possible to hypothesize a reduction in inappropriate prescriptions

due to a reduction of ambulatory visits for mild illnesses and a more frequent application of a waiting strategy for upper respiratory tract infection.

The major strength of the study is the overall evaluation obtained through the reimbursement database which entirely covers the population of residents in the Emilia-Romagna Region. Potential weaknesses are the lack of data on diagnoses and prescriptions made by private doctors, not reimbursed by the health system. The latter phenomenon should not have influenced consumption since access to this type of treatment should even be reduced during the lockdown.

The feared problem of an overuse of antibiotics due to the COVID-19 pandemic did not occur in Emilia-Romagna with regard to overall consumption in the community; nevertheless, a higher than expected use of azithromycin was observed, but it was probably related to the therapeutic uncertainty that characterized the first phase of the pandemic. In the future, it will be important to maintain attention and implement the necessary antimicrobial management strategies, adapting them to the pandemic context [7–10].

Disclosure statement

The authors report no conflict of interest.

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