Impact of recurrent COVID-19 disease waves on acute myocardial infarction epidemics : results from a regional network

Impact of recurrent COVID-19 disease waves on acute myocardial infarction epidemics: results from a regional network

Short title: COVID-19 disease and AMI

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ABSTRACT

Aims:

To assess the impact of COVID-19 related public containment measures during recurrent COVID-19 waves on hospital admission rate for acute myocardial infarction (AMI).

Methods and results

Clinical characteristics, reperfusion therapy modalities, COVID-19 status and in hospital mortality of consecutive AMI patients who were admitted in a regional AMI network were recorded during one year starting in March 2020 and were compared with the year before. The COVID-19 study period encompassed two waves: the first in March-May 2020 and the second in October-December 2020.

A total of 1349 AMI patients were hospitalized of which 725 during the pre-COVID period and 624 during the COVID period (incidence rate ratio of 1.16 , p=0,006). The impact was predominantly present in the first wave (32% reduction: n= 204 vs 152) and evanished during the second wave (3% increase (152 vs 156) . A similar pattern was observed for ACS with cardiac arrest with a 92% reduction (n=36 vs 3) during the first wave and no change during the second wave (18 vs 18). After correction for temperature and air quality, COVID-19 epidemic remained associated with a decrease of AMI hospitalization (p=0.046) Reperfusion strategy for AMI patients, were comparable between both study periods. The in hospital mortality between the two periods was comparable (2.6 % versus 1.9 %), but COVID-19 positive ACS patients (n=7) had a high mortality rate (14%).

Conclusion:

COVID-19 related public containment measures resulted during the first wave in a 32% reduction of AMI hospitalization, but this impact was not visible anymore during the second wave.

INTRODUCTION

The rapidly evolving coronavirus disease 2019 (COVID-19) pandemic has placed an overwhelming burden on health systems and authorities.[1] To mitigate the spread of the virus and gaining control of the epidemic's chains of transmission, governments have been taking compulsory measures to restrict all kinds of the congregation, and ensure the supply of living resources. Besides social distancing interventions such as closures of schools and the ban of all socio-cultural events, an increasing number of businesses and companies have asked their employees to work remotely. People are forced to stay at home and to restrict movement only for essential activities. Along with this public measures, hospitals had to establish effective systems for triage and essential care in emergency units and wards, including patient separation and staff safety.[2] Previous reports from the first COVID wave have documented a 15-40% reduction in admissions of AMI together with a significant delay in the treatment.[3-8]

The impact of this lockdown seems to be related at least partly to the fear of being hospitalized and being contaminated by the virus. In addition, strains on emergency transportation facilities, hospital infrastructures and the capacity of catheterization laboratories during the pandemic make timely revascularization challenging and may explain the treatment delays observed in many reports during the first COVID wave.

In the meantime, several COVID waves have been passed and to date, there are only limited reports describing the impact of recurrent COVID-19 waves on AMI epidemics. Does a better community awareness and a better hospital organization during a second wave reduces the fear to seek urgent medical and/or attenuates the risk of treatment delays as was seen during the first wave? Is there a rebound effect with higher admission rate of AMI between two COVID waves? Are changes in air pollution responsible for differences in AMI epidemics?

To answer these questions, we analyzed the AMI epidemics, treatment delays and environmental factors (such air pollution) in a regional AMI network during period of one year (march 2020 until February 2021) where two COVID waves occurred and compared this with a pre-covid period (march 2019 until February 2020).

METHODS

Study population and data collection.

The data were collected for consecutive AMI patients undergoing coronary angiography between 1 March 2019 until 28 February 2021 at the University Hospital of Antwerp. This hospital is the hub of a AMI networking with 3 spokes hospitals. The AMI network covers an area of 500.000 inhabitants. AMI is defined according to the Universal MI definition and includes ST elevation MI (STEMI), non STE elevation MI (nonSTEMI) and MI with no obstructive coronary arteries (MINOCA) .

For each patient, the following baseline characteristics, were retrospectively extracted from the hospital patient files: age, gender; cardiac risk factors; history of coronary artery disease (CAD) or peripheral artery disease (PAD); presence of chronic kidney disease, defined as eGFR<60 ml/min/1.73m², location of the infarction; cardiogenic shock at admission, cardiac arrest at admission, COVID status, in hospital mortality. In addition, for STEMI, time from onset of pain to diagnosis and time from diagnosis to treatment (wire crossing) were recorded. The study was approved by the ethical committee of the University Hospital of Antwerp.

COVID-19 epidemics

Official data about COVID-19 related hospitalizations in Belgium are retrieved from the National Scientific Institution in the Epidemiology of Infectious Diseases (Sciensano).

The first wave occurred in the period March-April-May 2020 and second wave was in the period October –November -December 2020.

The number of national COVID hospitalizations was taken as proxy for the severity of the COVID epidemic in the target area.

In all patients during COVID period a respiratory specimen was obtained to detect SARS-CoV-2 on a real-time reverse transcriptase– polymerase chain reaction assay (RT-PCR).

Environmental exposures

The pollutant concentration data used in this study were based on the air quality measurements realized by the Belgian Interregional Environment Agency (CELINE-IRCEL, http://www.irceline.be). The monthly mean (population weighted) concentrations for NO2, PM10, PM2.5 were calculated based on the daily mean interpolated concentrations using the RIO-model (4x4 km² resolution) in the province of Antwerp[9]. The monthly mean temperature was calculated based on the daily measurements in one telemetric monitoring station in Antwerp. To compare pre COVID period with the COVID period, the average of the 12 monthly data was calculated.

Statistics

Continuous variables are presented as means with the corresponding standard deviation (SD) or as median with interquartile range (IQR). Comparisons between groups were made using Student's *t*-test or the Mann-Whitney test for variables with a skewed distribution (cf. time delays). The differences between proportions were assessed by chi-squared analysis. The incidence rate of AMIs was calculated from the number of AMI admitted in the hospitals and the estimated population that was covered by the network (=500 000 inhabitants). Incidence rate ratio and 95% confidence interval for post versus pre COVID pandemic was reported. To determine risk factors for AMI hospital admissions negative binomial regression analysis was performed. Impact of temperature, PM2.5, PM10, NO2, O3 and COVID pandemic were first studied in univariable models. For the environmental factors mean, minimum or maximum were considered as a summary measure per month. The impact of the COVID pandemic is studied as binary factor (before/after march 2020) and as number of COVID hospitalizations. A final multivariable model was fitted to study the impact of COVID, after correction for the main environmental factors. This model included maximum temperature, maximum PM2.5 and COVID hospitalizations. To determine predictors of in hospital mortality, multiple logistic regression analysis was performed including following factors with at p value of <0.2 on univariable analysis: age, history of stroke, severe renal failure (defined as creatinine value of more than 2.0 mg/dl), AMI presentation (STEMI/nonSTEMI), COVID period and positive COVID test. For all analyses, a p value of <0.05 was considered statistically significant. All statistical analyses were performed using MedCalc Statistical Software version 13.0.6 (MedCalc Software bvba, Ostend, Belgium; http://www.medcalc.org; 2014) or R version 4.1.3 (R Core Team (2022). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/.)

RESULTS

COVID-19 epidemics in Belgium

Figures 1 shows the monthly event rate of covid-19 related hospitalization in Belgium from 1 March 2020 until 29 February 2021. The hospitalization rate due to infection outbreak showed two waves with one peak in April 2020 and the second peak in November 2020. The first wave is defined from March until May 2020, the second wave is defined from October until December 2020.

Study population

During the total study period, a total of 1349 consecutive AMI patients were admitted in the hospital of which 725 were admitted during the pre-COVID period and 624 during the COVID period. This corresponds with a incidence rate of 145/100000 inhabitants per year and 125/100000 inhabitants per year, respectively and with a incidence rate ratio of 1.16 (1.04 - 1.29, p =0.006)

The baseline characteristics of both study populations are described in table 1

There were no significant differences except for a higher prevalence of severe kidney failure, in the pre-COVID period. The distribution of STEMI , non-STEMI and MINOCA were identical. However, the presentation of ACS differs significantly with less ACS patients admitted in the covid period with cardiac arrest (8.8 vs 14%) or cardiogenic shock (2.2 vs 6.2 %). A total of 7 patients (1.1%) had a positive COVID-19 status during the COVID period

Environmental exposures

Average data of ambient particle concentrations, NO_2 and O_3 and temperature for the two study periods are shown in table 2. The environmental exposures were comparable across the study periods. Only ambient NO_2 concentrations were numerically lower during COVID period (15 ± 3.4 µg/m³ versus 18± 3.4 µg/m³ , p=0.06). Additional analysis revealed that reduction of NO_2 concentrations was greater during the first wave (13 ± 1.7 µg/m³ versus 18 ± 1.7 µg/m³ , p=0.04) than during the second wave (17 ± 3.4 µg/m³ versus 21 ± 3.2 µg/m³ , p=0.2)

Effect of COVID epidemic on AMI prevalence

Figure 2 depicts the evolution of AMI admission in relation to COVID epidemic. During the first wave there was a 32% reduction in admission rate (204/139) whereas during the second wave there was a 3% increase (152/156) (first versus second wave, p=0.001). There was no apparent increase of AMI admissions after the COVID wave. A similar pattern was observed for MI with cardiac arrest (see fig 3). During the first wave there was a 92% reduction in admission rate (36 vs3) whereas during the second wave no change in admission rate was observed (18 vs 18) (first versus second wave, p=0.0001)

Multivariable analysis revealed that COVID pandemic remained associated with a decrease of AMI hospitalization (IRR per 100 COVID hospitalization 0.998 , 95% CI 0.996-0.999) whereas air pollution (expressed by PM2.5 level) or temperature did not affect AMI hospitalization rate.

Reperfusion strategy and outcome

Reperfusion strategy in STEMI patients was predominantly primary PCI in both study groups (89% versus 88%). .

In STEMI patients the time delay between onset of pain and diagnosis was comparable between both study periods (median 109 min (IQR 85-133) before versus 103 min (IQR 80-158) during COVID (p=0.4). Also the door-to-balloon time was comparable between both study groups (median of 47min (IQR 35-68) versus 45 min (IQR 34-74), p=0.9)

The average in hospital mortality was 2.6% in the pre-COVID period and 1.8% during the COVID period (p=0.3). The in-hospital mortality was numerically lower during the first COVID wave as compared to the second wave (0% vs 1.9 %, p=0.1) Patients with concomitant COVID-9 infection had a higher mortality rate (14% vs 2.2%, p=0.15), but the number of patients with a positive COVID-19 status was limited. Multivariable analysis showed that high age was the most important independent risk factor of in hospital mortality (RR: 1,05; 95% CI: 1,019 - 1,090, p=0.002). COVID period was not associated with increased/decreased mortality.

DISCUSSION

The present study demonstrated that the dramatic containment measures to reduce the transmission rate of the virus during the first wave was associated with a 32% reduction of AMI admissions but this impact was not visible anymore during the second wave. The large reduction in AMI admissions (between 20 and 40%) during first COVID wave has been reported in many other countries and has been contributed to many possible mechanisms: first, the fear of contagion at the hospital with avoidance and denial behavior to seek urgent medical help in case of experiencing chest pain. Second, confusion of cardiac complaints with COVID-19-related symptoms and subsequent restraint from burdening the hospitals. Third, the focus of the EMS on COVID-19 with relocation of most healthcare resources to manage the pandemic. Finally, less exposure to external AMI triggers such as physical stress, high intensity physical activity, air and auditive pollution with subsequent a true reduction in the incidence of AMI[10].

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After the first COVID wave, health care systems have been gradually restored and containment protocols have been mitigated and adapted in order to guarantee better health care access of also non-COVID related disease. In addition, appropriate public campaign were set up to counterbalance the hospital avoidance behavior of people during this COVID-19 pandemic and to mitigate “collateral damage”. These measures seemed to have been successful as no apparent reduction in AMI admission was observed anymore during the second wave. A similar finding has been also recently documented by Solomon et al in United States of America. [11] This is a reassuring finding reflecting restored confidence of the patients in our health care system. Parallel to the mitigation of the containment measures, levels of air pollution after the first wave returned to pre-COVID values. As our multivariable model could not identify air pollution as an independent predictor of AMI admission, the effect of lower levels of air pollution during the first wave on triggering AMI’s seems not be clinically relevant in this short period of time, as was also documented in a recent publication[12].

Clinical characterization of the our study population revealed a dramatic reduction (>90%) in AMI with cardiac arrest during the first wave which evanished during the second wave. This finding most likely reflects the high threshold of bystanders and EMS to start cardiopulmonary resuscitation (CPR) and to transfer the patient to the hospital. This “selection bias” may also explain the very low mortality rate of 0% observed during the first wave.

Reperfusion strategy, including time delay did not differ between the COVID versus pre-COVID, whereas in other publications a delay of diagnosis and treatment was observed [7, 13]. In our AMI network the cancellation of most of the elective cardiac program during the first wave, guaranteed sufficient capacity and resources to keep offering the best evidence based care to our ACS patients and also after the first wave, hospital containment measures did not interfere with standard AMI protocol.

Only a minority (1.1 %) of the AMI patients had a positive COVID test, but there mortality was much higher (14%). In larger case series, the poor prognosis of AMI in patient with COVID-19 disease was related to a highly morbid state and/or to a prothrombotic state with higher instent thrombosis.[14]

The results of the present study should be considered in the light of following limitations.

We used the number of COVID hospitalizations as a proxy for the containment measures which may not reflect precisely the severity of containments measures but in general more stringent containment measures were applied during the COVID waves. Because of retrospective observational study design, not all baseline characteristics were available in the patient files For the multivariable analysis we selected only those with >80% availability and with at p value of <0.2 on univariable analysis. In addition, some important factors/triggers such as physical and mental stress were not captured in this study. We included only AMI patients that underwent coronary angiography in this study. Although our AMI network protocol recommends coronary angiography in all ACS patients with troponin rise, some AMI patients with severe comorbidity (such as sever renal failure, severe infection) might have been withheld from invasive evaluation, but we presume that the policy in those patients will be the same during both study periods.

In conclusion, COVID-19 related public containment measures resulted during the first wave in a 32% reduction of AMI hospitalization, but, this impact was not visible anymore during the second wave most likely thanks to a more focused public containment strategy, a better community awareness and a better hospital organization to cope with COVID-19 disease.

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Tabel 1: Clinical characteristics of the study populations

	Pre COVID	During COVID	P value
Number	725	624	
Age **Male, %** **BMI**	66±14 72 27±5	67±13 72 27±5	0.4 0.8 0.9
Diabetes, % **Renal failure, %** **Stroke, %**	25 6.5 14	28 2.8 15	0.3 0.007 0.6
Presentation **Cardiac arrest, %** **Cardiogenic shock,%** **STEMI, %** **nonSTEMI, %** **MINOCA, %**	 14.4 6.2 33 67 16	 8.8 2.2 33 67 15	 0.001 0.0004 0.9 0.9 0.9
Reperfusion therapy: **Primary PCI,** **Time diagnosis to balloon, min** **Door-to-balloon time, min**	 89 109 (IQR 85-133) 47 (IQR 35-68)	 88 103 (IQR 80-158) 45 (IQR 34-74)	 0.6 0.4 0.9
COVID +, %	0	1.1	0.004
In hospital mortality, %	2.6	1.8	0.3

Data presented as mean ± SD or median (IQR, interquartile range) .

Table 2. Temperature and air pollution levels in the two study period.

	Pre COVID	During COVID	P value
Temp., °C	12.5 ± 5.8	12.3 ± 5.2	0.9
PM 2.5, µg/m³	11.4 ± 3.7	11.3 ± 3.3	0.9
PM 10, µg/m³	19.8 ± 4.0	20.6 ± 4.5	0.7
O_3, µg/m³	46.7 ± 14.2	47.2 ± 15.3	0.9
NO_2, µg/m³	17.8 ± 3.4	15.1 ± 3.3	0.06

Data presented as mean ± SD.

PM_{10}: particulate matter with aerodynamic diameter<10µm; $PM_{2.5}$: particulate matter with aerodynamic diameter<2.5µm; NO_2: nitrogen dioxide; O_3: ozone ; Temp: temperature

Figure 1

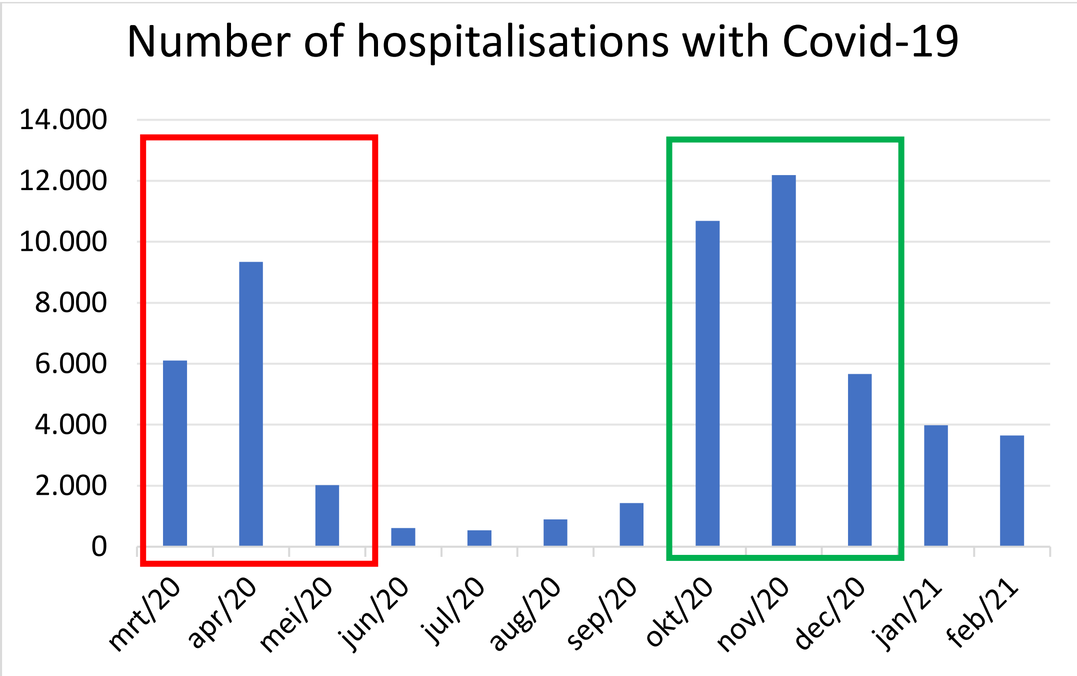
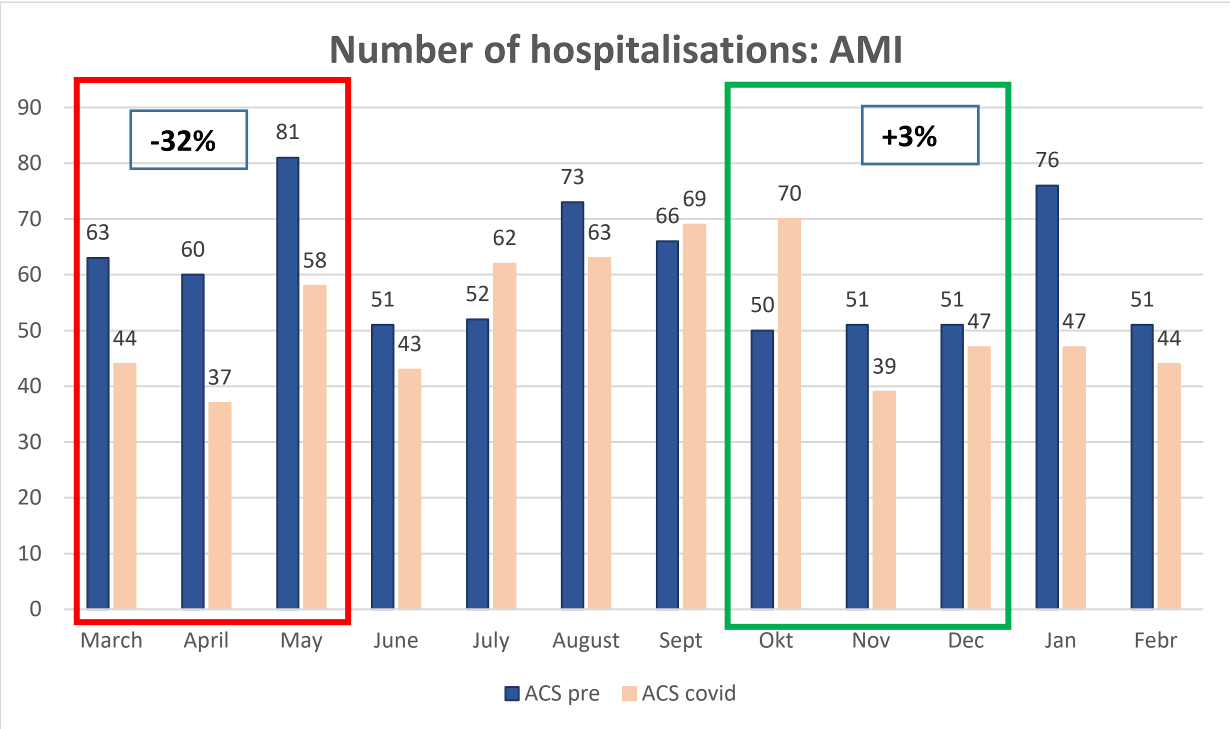


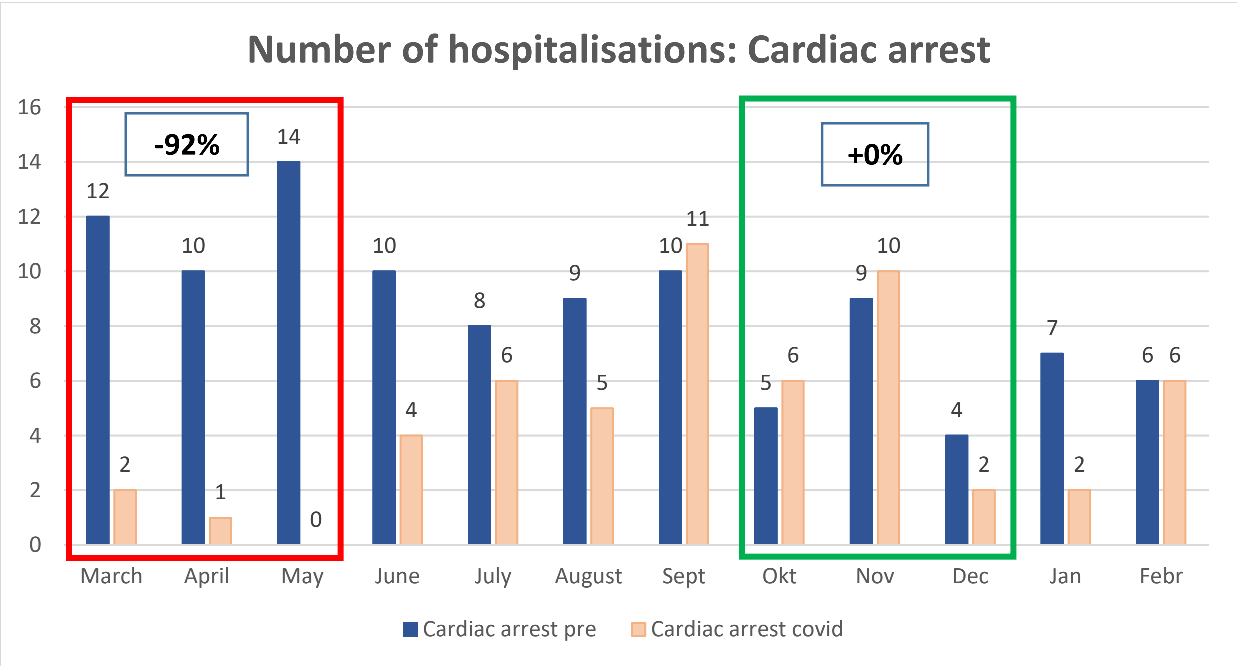
Figure showing event rate of covid-19 related hospitalization in Belgium with highlighting of the two waves.

Figure 2



Bar graph showing number of ACS hospital admissions per month in the pre COVID period (blue bar) and during COVID period (orange bar) . Red and green rectangle represent first and second wave, respectively. During the first wave there was a 32% reduction in admission rate whereas during the second wave there was a 3% increase.

Figure 3



Bar graph showing number of cardiac arrest hospital admissions per month in the pre COVID periode (blue bar) and during COVID period (orange bar). Red and green rectangle represent first and second wave, respectively. . During the first wave there was a 92% reduction in admission rate whereas during the second wave there was no change.

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