Different pattern of the second outbreak of COVID-19 in Marseille, France

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Short communication

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Philippe Gautret[1,2], Philippe Colson[1,3], Jean Christophe Lagier[1,3], Laurence Camoin-Jau[1,3,4], Audrey Giraud-Gatineau[1,3], Sophia Boudjema[1,3], Julie Finance[1,3,5] ,Hervé Chaudet[1,2], Didier Raoult[1,3,*]

1 IHU Méditerranée Infection, 19-21 boulevard Jean Moulin, 13005 Marseille, France;

2 Aix Marseille Univ, Institut de Recherche pour le Développement (IRD), Assistance Publique - Hôpitaux de Marseille (AP-HM), Service de Santé des Armées (SSA), Vecteurs - Infections Tropicales et Méditerranéennes (VITROME), Marseille, France;

3 Aix-Marseille Univ., Institut de Recherche pour le Développement (IRD), Assistance Publique - Hôpitaux de Marseille (AP-HM), Microbes Evolution Phylogeny and Infections (MEPHI), 27 boulevard Jean Moulin, 13005 Marseille, France;

4 Laboratoire d'Hématologie, Hôpital de la Timone, APHM, boulevard Jean- Moulin, 13005 Marseille, France

5 Assistance Publique de Marseille, Explorations Fonctionnelles Respiratoires, Aix Marseille Université, France.

* Corresponding author: Didier Raoult, IHU Méditerranée Infection, 19-21 boulevard Jean Moulin, 13005 Marseille, France. Tel.: +33 413 732 401, Fax: +33 413 732 402; email: didier.raoult@gmail.com

Running title: second outbreak of COVID-19 in Marseille

Abstract 169/200 words

Objective:

To describe the characteristics of COVID-19 patients seen in March-April and June-August, 2020 in Marseille, France with the aim to investigate possible changes in the disease between these two time periods.

Methods

Demographics, hospitalization rate, transfer to intensive care unit (ICU), lethality, clinical and biological parameters were investigated.

Results

Compared to those seen in March-April, COVID-19 patients seen in June-August were significantly younger (39.2 vs. 45.3 years), more likely to be male (52.9% vs. 45.6%), less likely to be hospitalized (10.7 vs. 18.0%), to be transferred to ICU (0.9% vs. 1.8%) and to die (0.1% vs. 1.1%). Their mean fibrinogen and D-dimer blood levels were lower (1.0 vs. 1.5 g/L and 0.6 vs. 1.1 µg/mL, respectively). By contrast, their viral load was higher (cycle threshold ≤16 = 5.1% vs. 3.7%).

Conclusions

Patients in the two periods did not present marked age and sex differences, but markers of severity were undoubtedly less prevalent in the summer period, associating with a 10 times decrease in the lethality rate.

Key words: COVID-19; seasonality; severity markers; lethality

794 words/800

Since its emergence in China at the end of 2019, SARS-CoV-2 spread worldwide with more than 29 Million cases of COVID-19 reported, as of 15 September, 2020. Currently, most cases have been reported from the US, India, Brazil and Russia (https://gisanddata.maps.arcgis.com/apps/opsdashboard/index.html#/bda7594740fd40299423467b48e9ecf6). In Europe, since the beginning of the pandemic, the EU/EEA and the UK have reported 1,733,550 COVID-19 cases and 182,639 deaths, as of 2 August, 2020 (10% of all cases reported worldwide). In early April, the EU/EEA and the UK reached a peak in reported cases. Then the trend declined until June to reach a plateau. however in recent weeks there has been a resurgence, although it is currently lower than the first peak which occurred in April [1]. In France, the incidence of PCR-confirmed cases peaked on early April with 50.1/100,000 and declined to less than 10/100,000 in early May, however, on late July the incidence rose again over this threshold and reached 75/100,0000 in early September [2].

In Marseille, the largest city in south of France and the second one in France, our institute adopted a strategy consisting in early and massive screening of SARS-CoV-2 infections and COVID-19 treatment using hydroxychloroquine and azithromycin, since the first case was documented. We recently described the characteristics of 3737 adult COVID-19 patients seen at our institute between 3 March and 27 April [3]. In this paper, we describe these characteristics in 743 new adult patients seen between 15 June and 15 August with the aim to investigate possible changes in the disease between these two time periods.

Starting from early March, our institute proposed massive testing of any person presenting at our facility regardless they had or not COVID-19 symptoms. On 16 March, the WHO Director-General called for testing every suspected COVID-19 case [4]. In France, the generalization of SARS-CoV-2 PCR testing was officially authorized by the Ministry of

Health on 4 May [5]. The number of individuals newly-tested at out institute for SARS-CoV-2 infection by PCR sharply increased from 765 per week in late February (week 9) up to 8105 per week at the peak at the end of March (week 13), and then progressively decreased to 1481 patients per week in early June (week 24) (**Figure 1**). It then increased again to reach 5007 per week on mid August (week 33). Interestingly, the proportion of individuals testing positive paralleled this curve with a slight shift of one week later. By contrast, numbers of deaths peaked to 33 per week during week 14 and progressively decreased to reach 0 week 24.

Compared to patients seen during late winter and spring, those seen in summer were significantly younger with a lower proportion of patients aged ≥65 years, and were more likely to be male, although differences were not marked (**Table 1**). No significant differences were seen with regards to anosmia and agueusia prevalence, according to period of study. Hospitalization rate, proportion of patients transferred to ICU, and lethality rates were significantly lower in patients seen in summer than in those seen earlier. The mean Ct value of positive PCR results was significantly lower in patients seen in summer than in those seen earler, with a proportion of patients with high viral load (Ct≤ 16) tending to be higher in summer. Lymphocyte and platelet counts and fibrinogen and D-dimer levels were significantly lower in patients seen in summer as compared to those seen earlier.

The current resurgence of COVID-19 in Marseille that started in June shows a marked dissociation between numbers of cases and numbers of death. The number of deaths among COVID-19 patients seen at our institute did not show a significant rebound, so far, while the number of cases clearly re-increased. Since the kinetic of the proportion of individuals testing positive paralleled the total number of tested individuals, the current increase in the number of new patients is not an artifact due to an increase in the number of tested individuals.

In this report we also show that the presentation of the disease in patients seen in summer is different than that of patients seen earlier. Patients in the two periods do not present marked age and sex differences, but markers of severity are undoubtedly less prevalent in the summer period, associating with a 10 times decrease in the lethality rate from 1.1 to 0.1%. At the time of writing, it seems, as described in other diseases [6], that the start of the epidemic was characterized by higher lethality rates, in comparison with the current phase of the epidemic. This could be possibly due to mutations of the virus. The current situation of the COVID-19 epidemic seems to be similar to that of other endemic coronavirus infections [7, 8]. Continuous analysis of epidemiological data is needed in the following months to confirm that this trend is continuous.

Author's note

Since this analysis was completed, and as of the 30 September 2020, 3557 additional patients were diagnosed at the Institut Méditerranée Infection with 33 deaths, resulting in an overall lethality rate of 0.8% in the 4325 patients seen between 15 June and 30 September 2020.

Competing interest

The authors declare that they have no competing interests.

Funding source

None

Ethical approval

Approval was not required

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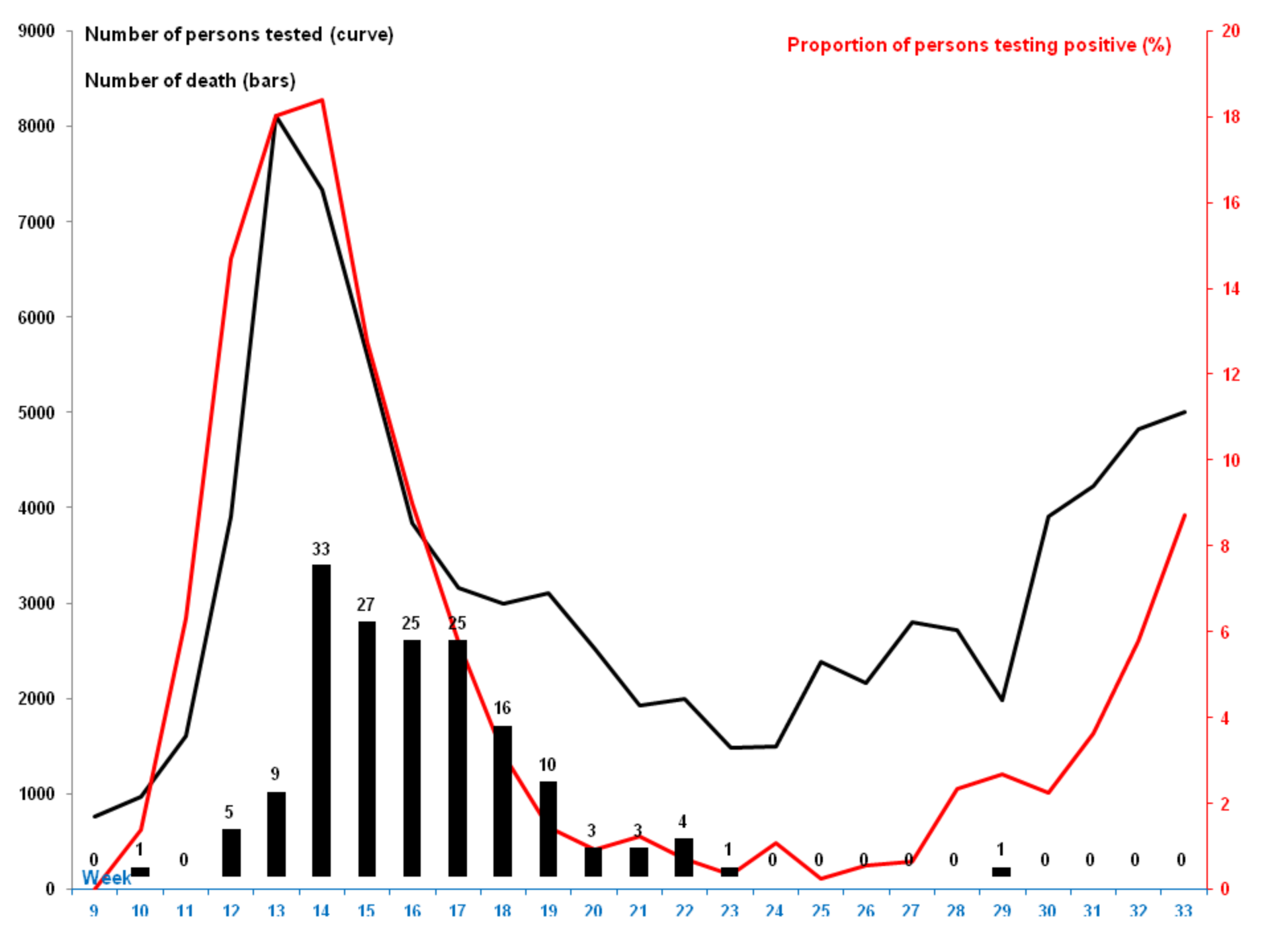
Legend to figures

Figure 1. Number of persons tested for SARS-CoV-2 (black curve), proportion testing positive (red curve) and number of death (black bars) in COVID-19 patients per week, at Méditerranée Infection Institute


Number of persons tested (curve)
Number of death (bars)
Proportion of persons testing positive (%)
9000
8000
7000
6000
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4000
3000
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1000
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Table 1. Characteristics of COVID-19 patients seen at Méditerannée Infection Institute according to seasons.

	Late winter and spring 3 March-27 April	**Summer 15 June-15 August**	**P value[1]**
N patients	3737	768	
Mean age	45.3 years Sd=16.8	39.2 years Sd=17.3	$<2.2\ 10^{-16}$
<65 years ≥65 years	3284 (87.9%) 453 (12.1%)	696 (90.6%) 72 (9.4%)	0.0358
Male sex	1704 (45.6%)	406 (52.9%)	0.00028
Hospitalization	673 (18.0%)	82 (10.7%)	$9.499\ 10^{-7}$
Transfert to ICU	67 (1.8%)	7 (0.9%)	0.048 (unilat.)
Death (all patients) Death (under 60 years)	41 (1.1%) 0 (0%)	1 (0.1%) 0 (0%)	0.0098 (unilat.) -
Anosmia	1442/3676 (39.2%)	249/644 (38.7%)	0.7931
Agueusia	1389/3676 (37.8%)	255/644 (39.6%)	0.4032
CT^2 value ≤16 at admission Mean Sd	113/3056 (3.7%) 25.0 5.3	36/700 (5.1%) 23.6 5.1	0.108 $4.051\ 10^{-10}$
Mean lymphocyte counts (G/L)	1.8 Sd=0.9	1.6 Sd=0.8	$1.15\ 10^{-6}$
Mean platelet count (G/L)	233.7 Sd=74.8	225.9 Sd=62.4	0.005

Mean fibrinogen blood level (g/L)	4.7 Sd=1.5	3.1 Sd=1.0	$< 2.2\ 10^{-16}$
Mean D-dimer blood level (µg/mL)	1.1	0.6	$2.8\ 10^{-16}$ (Wilcoxon)

[1]Fisher exact test was used to compare differences between proportions (unilateral test used when indicated). Quantitative data means were compared using Student's t-test or Wilcoxon's rank test.

[2]CT = cycle threshold