Clinical course of COVID-19 in a cohort of 342 familial Mediterranean fever patients with a long-term treatment by colchicine in a French endemic area

The novel COVID-19 pandemic caused by SARS-CoV-2 is responsible for many deaths worldwide. Severe or life-threatening disease induce an exaggerated inflammatory response known as the ‘cytokine storm’, raising the question of the susceptibility and severity of SARS-CoV-2 infection in patients displaying innate immunity disorders such as familial Mediterranean fever (FMF). Furthermore, FMF patients take a long-term therapy with colchicine, which has been tested in SARS-CoV-2-infected patients with conflicting results.¹

To tackle this question, we conducted a survey on SARS-CoV-2 infection in FMF patients followed in Paris area. In that meantime, the official French rate of infection in Paris area was 11% of the whole population.² FMF patients were identified from the juvenile inflammatory rheumatism (JIR) cohort, an international multicenter data repository and consented to the study. For the purpose of the study, we included only patients fulfilling the international FMF criteria, with a genetic confirmed FMF diagnosis,³ and followed up in the French national autoinflammatory centre in Paris area.

Identified patients (n=627) were invited to answer a short questionnaire in consultation by phone or email about a possible SARS-CoV-2 infection during the time span ranging from March until end of May 2020; 342 patients answered the survey SARS-CoV-2 infection, diagnosis had been retained if the patient displayed clinical symptoms with a positive SARS-CoV-2 reverse transcriptase (RT)-PCR or serology or a typical chest CT scan. Overall, 27 FMF patients (7.8% of the responders; sex ratio 1:1) contracted the virus and 315 did not. All but one of the FMF-COVID³ patients were taking daily colchicine since a median time of 23 years, mostly 1 mg/day table 1. Four received in addition an interleukin 1 (IL-1) inhibitor. Clinical symptoms of COVID-19 were consistent with those described previously.⁴

Out of the 27 FMF-COVID³ patients, 7 patients were admitted in hospital (25%), displayed and six required oxygen therapy 3 (11%) developed acute respiratory distress syndrome and went to intensive care unit for mechanical ventilation and haemodialysis (online supplemental table). Two patients died (7%) but had respectively three and four comorbidities for severe SARS-CoV-2 infection (see online supplemental table). The third patient, 40 years old, suffered from hypertension and obesity. Patient older than 65 years accounted for 17% of the whole cohort, 75% were hospitalised and required oxygen; one died. Out of the three AA amyloidosis patients, two were hospitalised and one died. No additional antiviral treatment was administrated. At the end of the first epidemic wave in Paris area, the five survivors after hospitalisation went back home. None of them showed clinical signs of FMF attacks during SARS-CoV-2 infection.

The profile of our patients with a severe or life-threatening SARS-CoV-2 infection was like the general population. Severe SARS-CoV-2 infection was seen only in patients displaying known risk factors such as advanced age, chronic kidney disease, hypertension, vascular disease obesity and lung dysfunction. Our study suggests that the dysfunction of the innate immune system of FMF does not seem to be a risk factor in itself. However, preventive effect of long-term colchicine intake cannot be concluded as it was reported in a large cohort of patients with continuous colchicine therapy.¹

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Total recovery</th>
<th>Recovery with persistent asthenia</th>
<th>Recovery with persistent dyspnoea</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>19</td>
<td>5</td>
<td>1</td>
</tr>
</tbody>
</table>

Table 1 Clinical course of 27 patients displaying COVID-19 in a cohort of 342 familial Mediterranean fever patients with a long-term treatment by colchicine in a French endemic area

<table>
<thead>
<tr>
<th>Age years, median</th>
<th>33 (17–87)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comorbidities</td>
<td></td>
</tr>
<tr>
<td>Age &gt;65 years old</td>
<td>6</td>
</tr>
<tr>
<td>Hypertension</td>
<td>4</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>2</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>4</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>2</td>
</tr>
<tr>
<td>AA amyloidosis</td>
<td>3</td>
</tr>
</tbody>
</table>

TNF, tumour necrosis factor.
treatment with daily colchicine have no additional risk factor for severe SARS-CoV-2 infection compared with the general population.

Rim Bourguiba 1, Marion Delplanque, Caroline Vinit, Felix Ackermann, Lea Savey, Gilles Gratteau, Veronique Hentgen, Sophie Georgin-lavialle 1

1 Sorbonne Université, AP-HP, D1M3ID, Tenon hospital, Internal medicine department, national reference center of autoinflammatory diseases and inflammatory amyloidosis (CEREMAIA), Paris, France
2 General pediatry department, Versaille hospital, André-Mignot, General pediatry department, National reference center of autoinflammatory diseases and inflammatory amyloidosis (CEREMAIA), versailles, france
3 Department of Internal Medicine, Hopital Foch, Sursennes, France

Correspondence to Professor Sophie Georgin-lavialle, Tenon Hospital, Internal Medicine, AP-HP, Paris 75020, France; sophie.georgin-lavialle@aphp.fr

Correction notice This article has been corrected since it published Online First. The author, Dr Ackermann, has been added to the author list.

Handling editor Josef S Smolen

Twitter Rim Bourguiba @Rimbourguiba1 and Sophie Georgin-lavialle @SophieGeorgin

Acknowledgements Pr Thomas Hanslik and Dr Philippe Evon.

Contributors All Authors contributed in writing the manuscript.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not required.

Ethics approval This observational study was based on data extracted from the Juvenile inflammatory Rheumatism (JIR) cohort, an international multicenter data repository established by the National Commission on Informatics and Liberty.

Provenance and peer review Not commissioned; externally peer reviewed.

Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

This article is made freely available for use in accordance with BMJ’s website terms and conditions for the duration of the covid-19 pandemic or until otherwise determined by BMJ. You may use, download and print the article for any lawful, non-commercial purpose (including text and data mining) provided that all copyright notices and trade marks are retained.

© Author(s) (or their employer(s)) 2021. No commercial re-use. See rights and permissions. Published by BMJ.

Additional material is published online only. To view please visit the journal online (http://dx.doi.org/10.1136/annrheumdis-2020-218707).

RB and MD contributed equally.


Received 27 July 2020
Revised 23 October 2020
Accepted 27 October 2020
Published Online First 2 November 2020


ORCID IDs
Rim Bourguiba http://orcid.org/0000-0002-7352-9074
Sophie Georgin-lavialle http://orcid.org/0000-0001-6668-8854

REFERENCES