



Chronic myelogenous leukaemia

## Prevalence of COVID-19 diagnosis in Dutch CML patients during the 2020 SARS-CoV2 pandemic. A prospective cohort study

Geneviève I. C. G. Ector<sup>1</sup> · Elisabeth G. W. Huijskens<sup>2</sup> · Nicole M. A. Blijlevens<sup>1</sup> · Peter E. Westerweel<sup>3</sup>

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### To the Editor:

We read with interest the article by Li et al. first to report on COVID-19 in patients with chronic myeloid leukaemia (CML) [1]. They found an increased COVID-19 prevalence in CML patients of the Hubei region in China when compared to the prevalence of the general population of that region. Unfortunately, in this retrospective study, follow-up data were not provided and a direct control group was not included.

We report preliminary results of a prospective Dutch observational cohort study that assessed differences in susceptibility for COVID-19 and severity of the disease course in adult CML patients and their adult housemates during the SARS-CoV2 pandemic (the first COVID-19 case was identified on February 27th in the Netherlands). Patients were invited to participate via CMyLife [2], a nationwide web-based portal focused on Dutch CML patients, from April 6th 2020 onwards. If available, their adult housemates (e.g., spouses) were included as control group, providing a better representation of the general population.

Surveys were performed at baseline and at a 2-weekly follow-up period. CML patients receiving TKI treatment or having a discontinuation of their TKI treatment were invited to participate. The study was approved by the Radboudumc institutional ethics committee and digital informed consent was obtained from both patients and partners.

At inclusion, information was gathered on demographics, self-reported comorbidity, vaccinations, health rating, COVID-19 related symptoms and hospital admissions and additional for patients; CML course, patients' perceptions regarding CML and COVID-19. Every 2 weeks a truncated shorter version of the questionnaire was conducted, focusing on TKI intake, preventive measures, testing, symptoms and hospital admissions.

At time of submission, 167 patients have registered for the study and 148 CML patients (median age, 57.5 years; range 26–82 years; 48% males) and 123 housemates (median age 60 years, range 24–88 years) were included, with enrolment still ongoing. The baseline characteristics are presented in Supplementary Table 1. The majority (88.4%) had taken TKI therapy.

Approximately half of the CML patients versus a third of controls had comorbidity that required medication. The annual influenza vaccination was received by 58.0% of the CML patients and 35.8% of their housemates. If a coronavirus vaccine would become available, both patients and their housemates would be largely willing to take this (76.3% and 68.9%, respectively). The majority applied preventive measures as recommended by national institutes (e.g., not shaking hands, frequently washing hands and social distancing). Patients' perceptions regarding COVID-19 are shown in Table 1.

Next we analysed symptoms of patients and housemates at inclusion (Table 2). Among patients, rhinitis was the most reported symptom (16.9%), followed by coughing (14.2%) and dyspnoea (10.8%). Fever was not reported. Many (69.6%) patients reported to be symptom free. Among the housemates, rhinitis was reported in 8.9% of cases, and coughing and dyspnoea in 6.5% and 2.4%, respectively. Again, fever was not reported. The majority (84.6%) reported to be free of symptoms. Only two patients had been tested for SARS-CoV2 at study inclusion, of whom one tested positive and reported to have been admitted to the hospital (without ICU admission). This patient was a 62 year male without comorbidity, who received imatinib therapy since the CML

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✉ Geneviève I. C. G. Ector  
genevieve.ector@radboudumc.nl

<sup>1</sup> Department of Haematology, Radboud University Medical Centre, Nijmegen, The Netherlands

<sup>2</sup> Department of Clinical Microbiology, Albert Schweitzer Hospital, Dordrecht, The Netherlands

<sup>3</sup> Department of Haematology, Albert Schweitzer Hospital, Dordrecht, The Netherlands

**Table 1** Reported perceptions of patients on COVID-19 related to CML.

	Patients ( <i>N</i> = 148) % ( <i>n</i> )
Thinks to be more susceptible to COVID-19 because of CML	
Yes	32.4 (48)
No	35.8 (53)
Do not know	31.8 (47)
Thinks COVID-19 course will be more severe due to CML	
Yes	35.8 (53)
No	20.3 (30)
Do not know	43.9 (65)
Worries about the coronavirus	
Not at all	5.4 (8)
A little	54.7 (81)
Quite a bit	30.4 (45)
Very much	9.5 (14)

diagnosis 2 years before. No housemates were tested nor reported any hospital admissions.

Currently, most subjects have completed their first and second 2-weekly follow-up questionnaires (Supplementary Table 2). No patients reported (temporarily) TKI discontinuation. A further six persons (two patients and four housemates) were tested for SARS-CoV2 during this follow-up and all tested negative. No hospital admissions were reported. At 2 weeks, 74.2% (*n* = 95) of the patients reported to be free of symptoms, compared to 79.4% (*n* = 100) and 88.9% (*n* = 16) at four and 6 weeks, respectively. For housemates these rates were 87.6% (*n* = 106), 91.6% (*n* = 98) and 100% (*n* = 15), respectively.

To conclude, we found no significantly increased prevalence of COVID-19 in CML patients. Only one patient (0.7%) reported to be tested positive and has been admitted to the hospital. These findings are important for CML patients and professionals (prescribers of TKI) as almost 40% of patients reported to be substantially concerned about the coronavirus. The prevalence rate is in line with the reported 0.3% in the general Dutch population [3], and with the reported low prevalence of <1% SARS-CoV2 viral infections in CML patients in the study of Li et al. We included a representative control cohort of housemates of similar age and geographical spreading as the patients, of whom none were tested positive (0%). Similar to Li et al. (0.9% vs 0.1%), we did find a slightly higher percentage of infected patients than in the general population (0.7% vs 0.3%) based on PCR testing on clinical indication, but this is not statistically significant. Other studies focusing primarily on COVID-19 infection prevalence in CML population are lacking.

**Table 2** Information on preventive measures, symptoms and hospital admissions related to COVID-19 in CML patients at inclusion.

	Patients ( <i>N</i> = 148) % ( <i>n</i> )	Housemates ( <i>N</i> = 124) % ( <i>n</i> )
Visited affected area <sup>a</sup>	3.4 (5)	4.1 (5)
Preventive measures <sup>b</sup>		
None	0	N/A
Avoid shaking hands	85.1 (126)	N/A
Clean hands often	84.5 (125)	N/A
Use of face mask	2.7 (4)	N/A
Working from home, just as same-function colleagues	31.8 (47)	N/A
Working from home, in contrary to same-function colleagues	6.8 (10)	N/A
Self-isolation	41.2 (61)	N/A
Other	14.9 (22)	N/A
Symptoms <sup>b</sup>		
Rhinitis	16.9 (25)	8.9 (11)
Coughing	14.2 (21)	6.5 (8)
Sore throat	4.1 (6)	2.4 (3)
Dyspnoea	10.8 (16)	2.4 (3)
Fever	0 (0)	0 (0)
No symptoms	69.6 (103)	84.6 (104)
SARS-CoV2 testing		
Tested, positive	0.7 (1)	0.0
Tested, negative	0.7 (1)	0.0
Not tested	98.0 (145)	100 (123)
Unknown	0.7 (1)	0
Hospital admission <sup>c</sup>		
Intensive Care Unit admission	0.0 (0)	0.0 (0)
Lives with adult housemate	85.9 (128)	–
	<i>N</i> = 131 % ( <i>n</i> )	<i>N</i> = 106 % ( <i>n</i> )
Vaccines		
Annual influenza vaccination		
Yes	58.0 (76)	35.8 (38)
No	42.0 (55)	64.1 (68)
If available, would take corona vaccine		
Yes	76.3 (100)	68.9 (73)
No	3.8 (5)	0.9 (1)
Do not know	19.8 (26)	30.2 (32)

<sup>a</sup>Affected areas with high risk of COVID-19 as established by National Institute for Public Health and the Environment: Italy, Austria, Nordrhein Westfalen (Germany), Madrid (Spain), China, South Korea, Iran.

<sup>b</sup>Multiple answers possible.

<sup>c</sup>Hospital/ICU admission because of the following symptoms: coughing, dyspnoea and/or fever.

There are strengths and limitations to our study. Although there may have been some self-selection bias in our study, the recruitment through the national CMyLife digital patient platform did allow for a substantial and geographically nationwide spread of participants, also in a time when many patients isolated themselves and hospital visits were limited when possible. Also, our study was performed prospectively, and included a control group. Furthermore, our questionnaires focused on patients' perceptions, offering insights in the substantial level of anxiety in this patient group. However, the number of SARS-CoV2 tested subjects was low, limiting statistical power.

Taken together, the report by Li et al. and our current data may offer relief to CML patients in general that the absolute risk of contracting a serious SARS-CoV2 infection in CML patients, was low (<1%) during the COVID-19 pandemic. However, as we did observe more upper airway symptoms and further research should focus on serological testing in the CML population to objectively assess subclinical COVID-19 infection prevalence. Finally, our study supports that patients can safely continue their TKI.

**Author contributions** GICGE and PEW designed the study; GICGE analysed the data; GICGE wrote the paper with contributions from all authors, who also interpreted the data, and read, commented on and approved the final version of the paper.

## Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

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