Long COVID among French Students: Results of the COVILON Study

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Abstract

Background: As we were alerted by students suffering a chronicle form of COVID19 infection we decided to make an inquiry on the long COVID among students known as being positive to COVID PCR.

Material and Methods: 1349 students known having been positive between August 2020 and July 2021 were asked, through their university emails, to fulfil an internet questionnaire from July 201 to October 2021. They were asked about their initial symptoms, the duration of symptoms, the impact of the disease on daily living activities and Health Related Quality of Life thanks to the SF36.

Results: Only 36.3% provided complete answers to the questionnaire. The prevalence of long COVID was 25.9% (at least 9.4%, considering the maximum bias of non-respondents), and 17.5% were still suffering at the moment of the survey. Women and chronically ill students had more frequently long COVID. We also were able to check the impact of long COVID on daily living activities as well as the important impact on quality of life, mainly on dimensions such as limitations due physical and mental health, and social well-being.

Conclusion: Although students have rarely severe forms of COVID, this disease has impact on their health which is not minor.

Background

Since the first lockdown in France, the University Health Services for Students have to manage the cases of COVID among students, which means to identify all the cases of COVID among students, to survey the intensity of symptoms and, in case to manage an hospitalization, to check the possibility of intra university cluster (due to the presence in classes or between classes) with the possibility to close temporarily (from 7 to 14 days) a curse in case of clusters among its attending students. In June 2021, we were contacted by students, mainly having important sport practices before the COVID lockdowns, suffering difficulties to reach the level of practices they had, due to problems such as being short of breath, extreme fatigue, tachycardia, while none of them were considered as having intense COVID symptoms and none were hospitalized. Some of them were sent to the rehabilitation assessment unit of the university hospital and were assessed for various effort mismatches.

At that time, the discussion about post covid symptoms was clearly in favour of something other then the maintenance of psychosomatic disorders [1-3], related to autonomic dysfunctions [4]. But, it was also poorly known in general population or in population non-hospitalized for COVID, and we decided to make an inquiry, among the students being positive between September and June 2021, to know the frequencies of post COVID syndrome, the nature of the problems the students face and if it could be useful to propose a specific track to readapt them to physical efforts. We present in this article the results of this inquiry, as there are very few data about long COVID in this type of population.

Materials and Method

There are 39 800 students having curses in the UCA (Université Clermont Auvergne, Auvergne area, south centre France). During the COVID outbreaks. Any graduate student at UCA (Auvergne-Rhône-Alpes, France) reported as positive after PCR testing ("confirmed case") for COVID-19 or suspected of being positive was contacted to locate their source case by trained investigators at UHS. The reports were made either by self-reporting on a dedicated email and/or form by the students, or by the teachers and/or the school because of an absence, or by the Regional Health Agency (Agence régionale de santé- ARH) after the positivity was registered in the national database of cases (SIDEP) based on laboratories declarations of every positive test. A collaboration was also set up with the Centre Régional des Œuvres Universitaires et Scolaires (CROUS) Clermont-Auvergne which had also information for the students it houses and was in charge of free catering for ill students. We kept in the database the only suspected cases secondary confirmed by a PCR testing. So, in our medical records, we had the identity of any positive students.

Medical records were protected for confidentiality according to the French laws and to the European General Data Protection Regulation. Detailed explanations about how worked the tracing for students were published elsewhere [5]. So, inclusion criteria were: being student in the UCA, having a positive PCR between August 2020 and July 2021. Students were contacted thanks to their university email, which is the main toll for giving information about classes schedules, examinations dates and results. They were asked to fulfil anonymously the questionnaire on an intranet form developed thanks to Lime survey.

The first announcement of the survey was so made by email on July 6th 2021, and there were 5 others relaunching emails up to October 1st 2021. The survey was anonymous. Students were free to participate. The questionnaire asked about the time of positivity, the existence of clinical signs at that time and after, and how long they lasted. According to the definition of the French medical authorities [6], used at that time, a long COVID was defined by the persistence other 28 days (4 weeks) of one of the following symptoms at the levels frequent/important or constant/major: myalgia, arthralgia, thoracic pain, dyspnoea, sleep disorder, headache, anosmia (complete or uncomplete) and ageusia (complete or uncomplete). We also asked the students about the activities they were used to do before the infection which became uneasy or impossible to do after (breathing, sleeping, eating, doing sport, shopping, driving, studying) in a scale 0 (no difference) to 3 (high impairment) scale. In case of dyspnoea, they had to fill-in the mMRC (modified Medical Research Council - scale (0 - dyspnoea only at effort, 1 during rapid walk, 2 usual walk, 3- need to stop after 100 meters walking, 4 –for daily efforts such a dressing/undressing). They also had to fill-in the Health

Quality of Life questionnaire SF36 in order to check their health-related quality of life. When appropriate the vaccination against COVID status was recorded (date, type of vaccine, number of doses), although, in France, the vaccination against COVID began only in April for students with chronic diseases and mid-June for the other students.

We also recorded the age, tobacco status, Student's localisation before entering the university. Statistical analysis (under SAS v9.4 (SAS Institute, Cary, NC, 2002-2012) computed the prevalence of declared long covid past and at the moment of the inquiry). We then compared students having still symptoms at the moment of the inquiry, those without symptoms but having declared a long covid, and those who never had any symptom. We used Chi-square tests for comparison, or non-parametric tests in case of short number of data. When comparing the three populations, we made first a global test and, if significant, a two by two Chi square tests. The alpha risk was 5%, bilateral. Results for the SF36 were compared to the sample of the French population of same age by [7] and a study by [8] among French students.

Results

Among the 1349 students identified as having had a positive PCR for COVID, 1317 had a correct email. 610 accessed to the questionnaire without fulfilling, 50 did not fully completed the questionnaire and 490 completed it leading to a 36,3% response rate (see flow chart in (Figure 1)). I is important to consider that none of the 1349 ill students had been hospitalized for a severe COVID infection. Students were tested positive 225.8 days before the survey (standard deviation 87,9 days, minimum 40 days). 113 (20,9%) had a variant of the SARS-COV2, mainly 201/501Y.
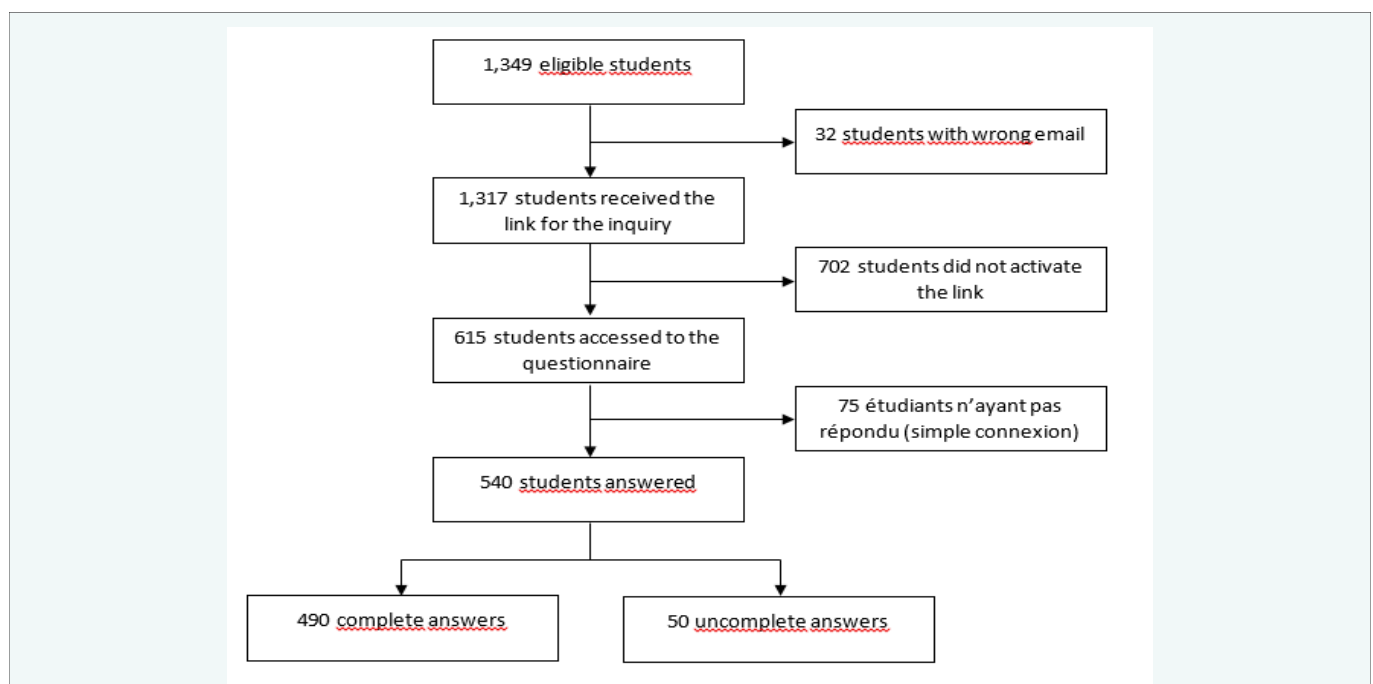

Figure 1 Flow chart.

V1 (n = 101). The characteristic of students are in (Table 1). They are close to the expected distribution, except a higher proportion of women (66% *vs* 56% expected) and of students with chronicle disease (5,7% *vs* 2,9%). 350 students (66.5%) were vaccinated at the moment of their answer, 85.7% by the Pfizer BioNTech (Comirnaty©). Only 5.7% had two doses, corresponding to the students with chronicle disease. 393 students (80.2%) experienced clinical signs when tested positive (Table 2). The five main symptoms were fatigue (78.6%), headache (64.4%), anosmia (60.6%), ageusia (51.4%) and fever (48.9%). Many students experienced prolonged symptoms, over 28 days: fatigue (23.4% of the students having fatigue initially), anosmia (35.6%), ageusia (31.8%), attention/ concentration disorder (which initially concerned 61 (15,5%) of the students, 47.3% keeping the symptom over 28 days) and difficulty to breath (initially 98 (24.9%), 24,7% over 28 days).

Table 1: Respondent characteristics.

n = 490	
Time between positivity to COVID and fulfilling the questionnaire (days)	
Mean (SD)	225.8 (87.9)
Min-Max	40-538
Médiane (Q1-Q3)	259.5 (144-282)
Sex, n (%)	
Masculin	163 (33.3)
Féminin	327 (66.7)
Age (years)	
Moyenne (SD)	21.8 (3.7)
Min-Max	18-54
Médiane (Q1-Q3)	21 (20-23)
BMI (kg/m²)	
Moyenne (SD)	22.7 (3.8)
Min-Max	14.5-44.1
Median (Q1-Q3)	22.0 (20.0-24.5)
WHO BMI classes, n (%)	
< 18.50	43 (8.8)
18.50-24.99	343 (70.3)
25.00-29.99	77 (15.8)
≥ 30.00	25 (5.1)
Chronic disease, n (%)	28 (5.7)
Tobacco, n (%)	
never	341 (69.6)
Occasionnaly	86 (17.6)
daily	45 (9.2)
Number of cigarettes per day	
Moyenne (SD)	7.4 (4.9)
Min-Max	2-20
Median (Q1- Q3)	5 (5 -10)
Stopped smocking	18 (3.7)
Since (years)	
Moyenne (SD)	3.1 (3.3)
Min-Max	0.08-12
Median (Q1-Q3)	2 (1-4)
Geographic origin, n (%)	
Europe	432 (88.2)
Africa	42 (8.6)
Middle Asia	3 (0.6)
Mayotte	5 (1.0)
South America	1 (0.2)
Oceania	1 (0.2)
East Asia	1 (0.2)
Other	5 (1.0)

SD: standard deviation; Min: minimum; Max: maximum; Q1-Q3: interquartile interval.

Table 2: Symptoms at the moment of the infection.

	n = 393 n (%)	Duration ≥ 28 jours a n/N (%)
Fatigue	309 (78.6)	68/290 (23.4)
Headache	253 (64.4)	16/236 (6.8)
Anosmia	238 (60.6)	80/225 (35.6)
Ageusia	202 (51.4)	62/195 (31.8)
Fever	192 (48.9)	1/184 (0.5)
Myalgia, arthralgia	169 (43.0)	6/159 (3.8)
Cough	157 (39.9)	13/146 (8.9)
Rhinitis	147 (37.4)	7/133 (5.3)
Chills	132 (33.6)	2/120 (1.7)
Breathing difficulties	98 (24.9)	23/93 (24.7)
Loss of appetit	91 (23.2)	7/85 (8.2)
Concentration/ attention problems	61 (15.5)	26/55 (47.3)
Sleep disorders	60 (15.3)	13/56 (23.2)
Thoracic pain	53 (13.5)	6/50 (12.0)
Diarrhea	40 (10.2)	4/37 (10.8)
Dizziness / Tinnitus	40 (10.2)	7/35 (20.0)
Nausea	36 (9.2)	3/34 (8.8)
Tingling / Numbness	30 (7.6)	1/24 (4.2)
Anxiety	28 (7.1)	9/27 (33.3)
Depression	19 (4.8)	7/17 (41.2)
Irritability	17 (4.3)	4/17 (23.5)
Memory loss	12 (3.1)	5/11 (45.5)
Vomiting	11 (2.8)	0
Itching / Urticaria	7 (1.8)	3/7 (42.9)
Constipation	6 (1.5)	2/5 (40.0)
Pseudo chilblains on hands and feet	3 (0.8)	2/2 (100)
Other	19 (4.8)	

On the whole, 140 students declared a long COVID (25.9% CI95% 22.2-29.6%). The prevalence of long COVID is 35.6% in case of initial clinical signs (CI95%: 30.9-40.4%). The symptoms were anosmia (57.1%), fatigue (48.6%), ageusia (44.3%), dyspnoea (16.4%), headache (11.4%), sleep disorders (9.3%) myalgia/arthralgia (4.3%) and thoracic pain (4.3%) (see table 2). 92 students (17,5%) were still declaring a long covid at the moment of the survey with the same profiles of clinical symptoms. Long COVID concerned more frequently the women (sex ratio (men/women) 0.22 for students experiencing long COVID, 0,51 for students having had clinical signs without long COVID, and 0.75 for students never been symptomatic p=0.0004) and students having a chronicle disease (12.2% for long COVID, 4.5% for symptoms without log COVID and 3.7% for asymptomatic). There was no difference in terms of age, geographic origin, body mass index and tobacco status, the time between the infection

and the moment of fulfilling the questionnaire, and the presence of a variant and immunization status.

92 students also declared that they expressed significantly more difficulties for daily living, as compared before the COVID infection. These students were mainly students recruited among students that have declared an initial long COVID (54.8%) compared to students having had symptoms during the infection (8:4%) and asymptomatic students (14.3%) ($p < 0.0001$). The level of difficulties concern little or moderate impairment (the maximum is a 1.5 quoting, on a 0 to 4 scale, for doing sport). The main differences concern sleeping, eating, walking, shopping, reading and studying. While the others domains are not significantly different, all the differences are in disfavour of students declaring a long COVID (Table 3). Quality of life was also significantly deteriorated for students experiencing a long COVID (Table 4). This concern mainly limitations due to physical and mental health, and social well-being.

Discussion

The assessment of long COVID in the general population remains complex. At the time of the survey, most of the studies concern hospitalized patients [9-11], and it is worthy to note that among our 1349 students, no one was hospitalized for a severe COVID disease, although some had chronicle illness such as diabetes, morbid obesity and chronicle inflammatory diseases (lupus, Crohn's disease, multiple sclerosis,) with various anti-inflammatory treatments. Only recently studies were made in the general population, not hospitalized [12-16]. But in these studies, very few is known for the population of students, young people from middle to high class; pursuing studies with a regular access to care. In a certain way, the only close study, in term of age and social class, concern athletes [17]. So, our study gives new insights on the consequences of the COVID infection in a large young and mainly healthy population, the students. The main defect of our study is a low response rate, at 36.3%. Although five reminders by email, the complete response rate is 36.3%, mainly because

Table 3: Intensity of higher difficulties for daily living before and after the COVID infection, at the moment of the survey.			
	Students with long COVID	**Etudiants without long COVID**	
	n = 48	n = 44	*p* -value
Breathing, mean (SD)	0.7 (0.9)	0.4 (0.6)	0.2626
Min-Max	0-3	0-2	
Sleeping, mean (SD)	1.0 (1.1)	0.5 (0.7)	0.0208
Min-Max	0-3	0-2	
Eating a, mean (SD)	0.6 (0.8)	0.2 (0.5)	0.0107
Min-Max	0-3	0-2	
Washing ourself, mean (SD)	0.2 (0.6)	0.0 (0.2)	0.1957
Min-Max	0-2	0-1	
Dressing, mean (SD)	0.1 (0.4)	0.0 (0.2)	0.2061
Min-Max	0-2	0-1	
Walking, mean (SD)	0.8 (0.8)	0.3 (0.6)	0.002
Min-Max	0-3	0-2	
Playing sport, mean (SD)	1.5 (1.1)	1.2 (0.7)	0.2242
Min-Max	0-3	0-3	
Shopping, mean (SD)	0.6 (0.9)	0.2 (0.4)	0.012
Min-Max	0-3	0-1	
Driving a, mean (SD)	0.2 (0.6)	0.0 (0.2)	0.0639
Min-Max	0-3	0-1	
Reading, mean (SD)	0.5 (0.7)	0.2 (0.6)	0.0132
Min-Max	0-2	0-3	
Studying, mean (SD)	1.3 (1.1)	0.7 (1.0)	0.0039
Min-Max	0-3	0-3	
SD: standard deviation; Min: minimum; Max: maximum; Q1-Q3: interquartile interval.			

Table 4: Health related quality of life (HRQoL) measured by SF-36 comparing students with long COVID at the moment of the survey, students who experienced COVID without prolonged symptoms, 18 to 24 years old population from the French sample for SF36 French version assessment by Leplège et al. [7], and students seen in systematic screening in a French university health service by Tran Qui et al. [8]

	Students with long COVID	Etudiants COVID+ without long COVID	18-24 years French population sample (Leplège)	Screened students (Tran Quy)	p (comparison : students with long covid to Leplège and Tran Quy samples)
	n = 90	n = 401	n = 326	n = 1082	
HRQoL dimension	mean	Δ	Δ	Δ	
Physical activity	81.1	95.1	95.5	95.9	< 0.001
Limitations due to physical health	60.4	90.2	91.6	82.2	< 0.001
Psychological well-being	48.8	63	67.5	-63.5	< 0.001
Limitations due to mental health	47.6	75	85.5	70	< 0.001
Vitality/ Fatigue	37	54.7	62.9	58.4	< 0.001
Social well-being	59.1	80.6	83	76.8	< 0.001
Pain	73.6	88.9	81.8	84.1	< 0.001
General Health	58.4	74.1	75,3	72.1	< 0.001

52% of the students did not consider our emails. In consequence, respondents were more frequently females and having chronicle disease (although they only represent 5.7% of the answers). This can have skewed our results.

Meanwhile, if we consider that 25.9% of the answers reported long COVID, and if we applied the rule of maximum bias due to non-respondents (supposing that all the non-respondents were perfectly healthy, it means that 9.4% of the students had long COVID, which is over the results of surveys in general population, in France (4% [14]) as well as in other countries (6% in Scotland [13], 5.5% in Netherlands [15], 4.6% in Israel for the main symptom [17]). And it is a minimal rate, it is very probable that there are still ill students among the non-respondents. The same computation can be made to estimate the proportion of students still suffering when we investigated them. So, at least 6.4% were still suffering more than 40 days after the infection (on average 225 days after the initial infection). 80.2% of the students experienced clinical symptoms when they had the COVID infection. The main symptoms are close to what is reported in the general population [12-16] with very common symptoms (fatigue, headache, fever) and more typical ones (anosmia and ageusia). The main clinical signs of the 25,9% of students experiencing long COVID are roughly the same, showing the same level of importance of some specific health problems, in general population as well as hospitalized patients, such as anosmia and ageusia [18]. Some specific but less frequent symptoms, such as tinnitus, are find at the expected level [19]. The main factors related to having a long COVID are being a woman and having clinical signs during the initial infection.

At the moment of the inquiry, 17.5% still suffer clinical symptoms, although the minimal time between the moment of the infection and the survey was 40 days. The same proportion declared to have greater impairment at the moment of the inquiry, in daily living, since the disease. Most of the impairment concern the fatigue, and very common symptoms. We have also measured the Health-Related Quality of Life, and it shows the same global deterioration for students having long COVID. There is still the question to understand if it is really a specific consequence of the COVID infection, if it is related to the general deterioration of psychological status of the French students since the first lockdown [20]. But, there is a clear difference with the students who had no clinical symptoms at the initial infection. Even if these asymptomatic students declare a worst daily living after the infection, showing the global impact of the disease and its general consequences, such as lockdown, the students having a long COVID are much more affected. We can hypothesize that the difference between long COVID and non-long COVID students represent the effective impact of the chronicity of the disease. This is consistent with studies showing psychological and neurological impacts of the disease [21], worsened in case of preexisting fragilities [22].

We did not measured the protective impact of vaccination, that is due to that the vaccination campaign for non-chronically ill students began only on the second half of July -and none of them got sick after the beginning of July, in our database. Also, 6 (in July) and 4-month (in September) delay was respected for the very first immunization. Except for chronically ill students, who could get vaccination in April with a quicker plan for first and second immunization, but they represent only 5.7% of our study. The impact on quality of life is particularly. It is the first using as indicator of impact the measure of quality of life thanks to generic standardized measure- the SF36, and are able to compare the results to surveys in the same population, long before the COVID outbreak. While students without long COVID have profile close to the two samples of general population, students suffering long

COVID have a significant lowering of their quality of life, mainly for psychological well-being, limitations due to mental health and vitality/ fatigue.

We were really surprised by the high prevalence of long COVID and the remaining symptoms at the time of the inquiry. As the study was planned in order to decide if specific actions are required, we choose to create a specific program for the chronically ill students. It contains a global information about the reality of clinical impacts of long COVD, saying that it was not just a simple psychosomatic problem and to present the possibility of rehabilitation, mainly based on relearning of physical effort. We created a special fast track for evaluation (medical consultation, and physiological and effort testing) and care the suffering students (by a rapid access to rehabilitation daily hospital, and, if appropriate, to other structures to solve the other problems, such as chronicle pain, rehabilitation of smell and taste). Information were sent through university intranet, social networks, as well as local media, particularly the radios listened by students. As our inquiry was totally anonymous, we were not able to focus the information to the most ill students. Another problem is that the hospital systems, both public and private, have to face an important and chronicle crisis, saturating every medical facility, so that taking care of students and building a specific information system to show how the track works was a very secondary priority.

It is also possible to consider that between the time of the inquiry (from July to October 2021 and the delay for publishing the very first results (as soon as August) and the building of a specific fast track, made that our proposal, since late October 2021 was too late for many students. First, the proportion of long COVID decrease from 25.9% immediately after the initial infection to 17.5% and this decrease must have continued over time. Second, recent data from Israel shows that most of the chronicle troubles due to long COVID stop a year later [16]. Anyway, our study reveals the importance of the clinical consequences for student. If no one was hospitalized due to COVDI at that time, it was an important argument to promote vaccination for the students. Based on the preliminary results of August, we developed a summer campaign promoting vaccination which is a part of the rapid success of vaccination among our students, along with stronger initiative such as sanitary pass to access to collective closed places (cinema, café, swimming pool,). When making our promoting campaign for vaccination we had to face many antivax reactions, even from inside the university, but never from students. At the end of November, the vaccination rate was over 98%.

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