Timing of Onset of Symptom for COVID-19 from Publicly Reported Confirmed Cases in Uganda

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Abstract

**Background:** The incubation period for COVID-19, which is the time from exposure to symptom onset, is on average five to six days but reach 14 days. The question is, the timing of onset of various signs and symptoms of COVID-19 along the period amongst cases in Uganda is not known.

**Methodology:** We utilized administrative data of publicly reported real-time RT-PCR laboratory COVID-19 confirmed cases in Uganda to investigate the timing of symptom onset, from 21-Marto 4-Sep-2020. Since timing of COVID-19 symptom onset is highly likely to be an interval rather than a point estimate, we generated three tertile categories of the period – 1st, 2nd, and 3rd tertiles denoting symptom presentation within 3, 4-6 and at least 7-days respectively. All signs and symptoms reported in the database were considered. We did not make any inferences about asymptomatic infection with SARS-COV-2. We analysed using frequency distributions, Chi-square test and Multinomial Logistic Regression; and controlled for age and sex.

**Results:** We analysed a total of 420 symptomatic case-patients. The case-patients were predominantly male, 72.0% (304/420), median age of 33 years, IQR=26-41. The common symptoms of SARS-CoV-2 were: cough (47.6%), running nose (46.2%), fever (27.4%), headache (26.4%) and sore throat (20.5%). We utilized only 293 COVID-19 symptomatic cases that had clinical symptom onset date recorded for analysis of the timing of symptom onset. Most case-patients, 37.5% (109/293) - presented symptom within 3-days after laboratory confirmation, 31.4% (92/293) had symptoms in the 2nd and another 31.4% (92/293) in 3rd tertile, denoting 4-6 days and at-least 7 days after exposure, respectively. Running nose (RRR =0.45, 95% CI 0.24 - 0.84) and chest pain (RRR = 0.64, 95% CI 0.09 – 0.72) were less likely to occur in the 1st tertile and 2nd tertile rather than in the 3rd tertile. Case-patients aged ≥20yrs were less likely to have symptoms in the 1st and 2nd tertile compared to ≤20 years (p < 0.05).

**Conclusion:** Our study provides empirical evidence for epidemiological characterization of cases by signs and symptoms along the incubation period among case-patients. This complements the current proposals for the length of active monitoring of persons exposed to SARS-CoV-2.

Background

The outbreak of the novel coronavirus disease (COVID-19) caused by Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV-2) was first reported in Wuhan City, China in December 2019 but quickly spread across the world by travelers who originated from or passed through COVID-19 hotspots. On 30th January 2020, the Emergency Committee convened by the Director General of the World Health Organization under the International Heath Regulations (2005) declared the COVID-19 outbreak a Public Health Emergency of International Concern (PHEIC)(1,2). Shortly afterwards, COVID-19 was declared a pandemic ravaging the world. Africa’s first COVID-19 case was recorded in Egypt on 14th February 2020 and many other African countries begun registering cases through travelers returning from hotspots in Asia, Europe and the United States (3).

Uganda reported its first case on the 21st March 2020 – a traveler who entered the country a day before on an international flight and got screened at Entebbe International Airport(4). The Government of Uganda (GoU) responded early by instituting multiple escalated strategies to curb the spread of COVID-19, but the country still experienced an upward trend as the epidemic evolved; reaching 6,468, with 63 deaths and 2,731 recoveries by 22nd September 2020 (5).

Development of symptoms has been documented to occur between 2 to 14 days in a number of studies across the globe (5). The World Health Organization (WHO) defines the average incubation period for COVID-19 as 5–6 days,
however it could go up to 14 days(2)… Imperial evidence based on 88 confirmed cases in Chinese provinces outside Wuhan shows similar findings regarding the mean incubation period(3). Using data on known travel to and from Wuhan, the study indicated a mean incubation period of 6.4 days (95% CI, 5.6 to 7.7 days). Further, Linton et al.’s (2020) study based on 158 confirmed cases outside Wuhan established similar findings regarding timing of symptom onset. A median incubation period of 5.0 days (95% CI, 4.4 to 5.6 days) was established in their study, with a range of 2 to 14 days (4). The role of the incubation period is explained by Lauer et al. (2020) as follows: “The incubation period can inform several important public health activities for infectious diseases, including active monitoring, surveillance, control, and modeling” (5). In particular, the length of active monitoring needed to limit the risk of contracting SARS-CoV-2 infection is vital in curtailing direct and indirect transmission of COVID-19.

Transmission of SARS-CoV-2 from a pre-symptomatic case can occur before symptom onset. Nevertheless, infection with SARS-COV-2 can be asymptomatic or may result in mild to severe symptomatic disease(1). It is important to note that transmission of SARS-CoV-2 from a person can occur while they are experiencing symptoms. This occurs when non-infected persons get in direct contact with infected symptomatic people through respiratory droplets or by contact with contaminated objects and surfaces (8–10). The time of symptom onset is critical as one may be more contagious when compared to later stage of the disease(2,11).

While there seems to be a consensus regarding the incubation period for COVID-19 ranging between 2 to 14 days (2–4), the questionable aspect however is: (i) empirical evidence on the timing of particular signs and symptoms of COVID-19 along the period; (ii) timing of symptom onset for various characteristics of cases. Following recommendations by the WHO on surveillance for COVID-19, Uganda monitored cases and contacts for signs and symptoms of COVID-19 as a procedural requirement. Further, specimens were taken and tested in a laboratory to confirm the SARS-CoV-2 infection status of the individuals (3). To this end, maintaining records on the cases and contacts as well as procedural aspects undertaken became a necessity. However, the WHO recommendation on surveillance at the primary care level stipulates that only the minimum number of data variables should be collected which include age, sex, date of illness onset, date of sample taken, test result, and location of testing site(11). The data has primarily been used by countries (Uganda inclusive) for monitoring and managing cases. Hardly any comprehensive analysis of the data has been undertaken to inform epidemiological categorization, including identification of clinical features of cases along and after the incubation period of COVID-19. It’s important that policy makers and public health experts pay attention to evidence available in the country to implement interventions on COVID-19. Using laboratory confirmed symptomatic cases of COVID-19 in Uganda, our study provides empirical evidence concerning the incubation period particularly focusing on timing of symptom onset.

**Methods**

We used administrative data from publicly confirmed cases in Uganda who developed symptoms of COVID-19 to investigate the timing of symptom onset. The investigation covered the following signs and symptoms: Fever, cough, sore throat, shortness of breath, headache, chest pain, running nose; nausea, vomiting, abdominal pain, muscle pain and joint pain; diarrhea, chills and general body weakness. In addition to the signs and symptoms, we controlled for demographic characteristics of the cases namely age and sex. This is because studies on COVID-19 patients have shown that higher risk of development to the severe form of the disease and fatalities is more likely among men when compared to women (12–16). It is important to note that our study does not make any inferences about asymptomatic infection with SARS-CoV-2. This study was a descriptive exploratory analysis of publicly reported confirmed cases of COVID-19 in Uganda. The cases were laboratory-confirmed for the COVID-19 infection by real-time RT-PCR between March 21st 2020 and September 4th 2020. All the cases were monitored for any indication of signs and symptoms of COVID-19 before and after specimens were taken to ascertain their status(17,18). For the purpose of this study, we
utilized only 420 cases that presented at least a sign or symptom of COVID-19. The symptomatic cases represent 32.6% of the overall number of complete cases in the dataset (n = 1,288). The least common symptoms were excluded from the analysis in the subsequent sections. This is because numbers of individuals who presented with the symptoms were relatively small (n ≤ 25) for any meaningful statistical inference to be obtained from the data.

**Variables and their measurements**

Timing of symptom onset for COVID-19 was considered as the outcome variable. We defined timing of onset of symptoms as a period between date when case was confirmed positive for COVID-19 using laboratory test results to the date of clinical onset of any signs and symptom. The variable denotes the period between date when case was confirmed positive for COVID-19 using laboratory test results to the date of clinical onset of any signs and symptom. Overall, the period ranges between 0 to 14 days. The number of days each of the three categories adopted in investigating the timing of symptom onset were: 0–3 days in the 1st tertile, 4–6 days in the 2nd tertile and at-least 7 days in the 3rd tertile. Time zero (0) denotes cases that were clinically identified symptomatic on the same day when they were confirmed positive for the SARS-CoV-2 virus. Based on the dearth of clinically available documented evidence on how the incubation period could be appropriately categorized, we automatically generated three quantile categories using the `xtile` command in STATA 15.0. Each of the two points that divide the distribution (i.e. the incubation period) into three parts - each containing a third of the population - is referred to as a tertile. It is evident that the incubation period was investigated in our study using a normal outcome i.e. symptom onset occurred either in 1st tertile, 2nd tertile or 3rd tertile. This is because it is highly likely that the time for symptom onset would statistically be an interval rather than a point estimate. This background forms the basis behind using a categorical outcome to establish the period or days within which particular symptoms would occur. The explanatory variables were: (i) status of onset of symptoms for COVID-19 namely cough, sore throat, shortness of breath, headache, chest pain, running nose, nausea, vomiting, abdominal pain, muscle pain and joint pain, diarrhea, chills and general body weakness; (ii) demographic characteristics of cases namely age and sex.

**Data Analysis**

The analysis was carried out using STATA 15.0 at three stages: First, a descriptive summary of the demographic characteristics of cases (age, and sex), status of symptoms of COVID-19 and timing of onset of first symptoms was done using frequency distributions. Second, differentials in timing of symptom onset were assessed by characteristics of cases and status of onset of symptoms of COVID-19 using cross-tabular analysis. Associations were established using the Pearson Chi-square test. For the purpose of this paper, all variables that presented a relatively low probability value following the Chi-square test (p < 0.5) were considered for further analysis unless otherwise stated. Third, the timing of symptom onset was investigated at the multivariable stage using a Multinomial Logistic Regression (MLR). The model investigated the risk of symptom onset during: (i) 1st tertile (0–3 days) rather than 3rd tertile (beyond seven days) after laboratory confirmation for COVID-19; (ii) 2nd tertile (4–7 days) rather than 3rd tertile (beyond seven days) after laboratory confirmation for COVID-19. The base category in the MLR was 3rd tertile i.e. beyond seven days of laboratory confirmation for COVID-19. In addition to the symptoms for COVID-19, we utilized demographic characteristics of cases namely age and sex. The MLR model was assessed for appropriateness using model fit statistics obtained via the `fitstat` command. [13, 14]. In particular, we utilized the Akaike information criterion (AIC) and Bayesian information criterion (BIC) to compare different possible models and determine which one was the best fit for the data. A lower AIC or BIC value indicated better fit – model that explains the greatest amount of variation using the fewest possible independent variables.
Limitations Of The Study

Similar to the challenges of administrative data elsewhere, the data had missing information. Thus, we utilized data with complete information for the variables of interest to address the issue. In addition, we did some data cleaning to correct any internal inconsistencies that existed in the data. For example, some cases had erroneously been regarded as asymptomatic yet a date of clinical onset of symptoms and presentation of signs and symptoms were captured in the database.

Results

Characteristics of symptomatic cases

By September 4th 2020, a total of 1,288 complete records of publicly reported confirmed cases for SARS-CoV-2 infection were available in the dataset. A total of 420 out of the 1,288 cases were symptomatic. Case-patients were predominantly male (72.4%), median age was 33 years (Interquartile Range (IQR) = 26–41); the highest proposition were in their 30s with regard to age (36.4%), followed by those aged 20–29 (25.1%) and 40–49 (14.9%) while the rest were either above 49 (13.0%) or below 20 (10.6%) years.

Table 1
Demographic characteristics of cases assessed in the study

| Characteristics | Frequency [n = 420] | Percentage (%) |
|----------------|---------------------|----------------|
| Age            |                     |                |
| 19 Below       | 44                  | 10.6           |
| 20–29          | 104                 | 25.1           |
| 30–39          | 151                 | 36.4           |
| 40–49          | 62                  | 14.9           |
| 50 Above       | 54                  | 13.0           |
| Total          | 415                 | 100.0          |
| Sex            |                     |                |
| Male           | 304                 | 72.4           |
| Female         | 116                 | 27.6           |
| Total          | 420                 | 100.0          |

Note. Median age is 33 years, Interquartile Range (IQR) = 26–41 years; variations in totals is due to missing data; 24 out of the 420 cases (5.7%) were aged 60 years and above.

Onset of symptoms for COVID-19

The commonest symptoms among the 420 case-patients who presented with symptoms were: cough (47.6%), running nose (46.2%), fever (27.4%) as well as headache (26.4%) and sore throat (20.5%). The least common symptoms were vomiting (0.5%), diarrhea (1.0%), nausea (1.9%) as well as muscle pain (3.8), abdominal pain (4.1%) and joint pain (4.3%) (Fig. 1).
Timing of symptom onset for COVID-19

Despite the timing for symptom onset being treated as a nominal outcome using three categories, it is important to note that median time to symptom onset was 5.0 days (range, 0–14 days, IQR = 2–8). The distribution of the time to symptom onset is presented in Fig. 2. The illustration shows that the highest proportion of cases (37.5%) presented symptom(s) within the three days after laboratory confirmation for the SARS-CoV-2. The rest presented symptoms either in the 2nd tertile (31.4%) denoting 4–6 days or 3rd tertile (31.4%) denoting at-least 7 days after being confirmed positive for SARS-CoV-2.

Differentials in timing of symptom onset

Table 2 presents a cross-tabular analysis of differentials in timing of symptom onset. It is important to note that only cases where a symptom is presented are shown in the table. In the results, the common symptoms in the 1st tertile were: sore throat (44.6%), fever (41.2%), shortness of breath (36.4%) and cough (34.9%). Running nose (33.9%) was the common symptom in the 2nd tertile denoting 4–6 days after exposure to the virus. The common symptom in the 3rd tertile - beyond six days after laboratory confirmation for COVID-19 - were chest pain (51.2%), general body weakness (43.9%), headache (39.7%) and cough (37.1%).
Table 2
Differentials on timing of clinical onset of symptoms for COVID-19

| Characteristics of Cases | Frequency | Timing of symptom onset [%] | Chi2  | p-value |
|--------------------------|-----------|-----------------------------|-------|---------|
|                          |           | 1st Tertile | 2nd Tertile | 3rd Tertile |       |       |
| Demographics             |           |       |       |        |       |       |
| Sex                      |           |       |       |        |       |       |
| Male                     | 215       | 37.2 | 30.7 | 32.1 | 0.250 | 0.882 |
| Female                   | 78        | 37.2 | 33.3 | 29.5 |       |       |
| Age group                |           |       |       |        |       |       |
| 19 Below                 | 35        | 42.9 | 48.6 | 8.6  | 14.60 | 0.067 |
| 20–29                    | 74        | 37.8 | 31.1 | 31.1 |       |       |
| 30–39                    | 101       | 34.7 | 30.7 | 34.7 |       |       |
| 40–49                    | 41        | 41.5 | 29.3 | 29.3 |       |       |
| 50 Above                 | 39        | 33.3 | 20.5 | 46.2 |       |       |
| Signs and Symptoms       |           |       |       |        |       |       |
| Fever                    | 89        | 41.2 | 23.5 | 35.3 | 3.44  | 0.148 |
| Cough                    | 145       | 34.9 | 28.0 | 37.1 | 3.73  | 0.155 |
| Sore throat              | 56        | 44.6 | 23.2 | 32.1 | 2.51  | 0.284 |
| Shortness of breath      | 33        | 36.4 | 27.3 | 36.4 | 0.50  | 0.779 |
| Headache                 | 68        | 27.9 | 32.4 | 39.7 | 4.01  | 0.134 |
| Chest pain               | 41        | 31.7 | 17.1 | 51.2 | 9.46  | 0.009 |
| Running Nose             | 130       | 30.0 | 33.9 | 36.2 | 5.38  | 0.068 |
| General Body Weakness    | 41        | 31.7 | 24.4 | 43.9 | 3.50  | 0.173 |

Note. Variations in number of symptomatic cases is due to missing data; timing of symptom onset – evaluated in days – refers to 1st, 2nd and 3rd Tertile

Predicting timing of symptom onset

The risk of symptom onset in the 1st tertile - rather than in the 3rd tertile - was significantly associated with age and running nose (p < 0.05). These findings can be explained as follows: Cases aged 20–29 (RRR = 0.21, 95% CI 0.05–0.87), 30–39 (RRR = 0.20, 95% CI 0.05–0.81), and above 49 (RRR = 0.13, 95% CI 0.02–0.61) were less likely to have symptoms in the 1st tertile rather than in the 3rd tertile compared to those aged below 20 years. Cases with running nose were less likely to present the symptom within the 1st tertile rather than in the 3rd tertile compared to those without (RRR = 0.45, 95% CI 0.24–0.84). Although marginally significant, it is worth noting that headache (p = 0.065) and chest pain (p = 0.052) were less likely to present in the 1st tertile rather than the 3rd tertile.
The risk of symptom onset within the 2nd tertile - rather than in the 3rd tertile - was significantly associated with age and chest pain (p < 0.05). These findings can be explained as follows: Cases aged 20–29 (RRR = 0.20, 95% CI 0.04–0.83), 30–39 (RRR = 0.18, 95% CI 0.04–0.72), 40–49 (RRR = 0.20, 95% CI 0.04–0.92) and above 49 (RRR = 0.09, 95% CI 0.01–0.47) were less likely to have symptoms in the 2nd tertile rather than in the 3rd tertile compared to those aged below 20 years. Chest pain was less likely to present within the 2nd tertile rather than in the 3rd tertile compared (RRR = 0.26, 95% CI 0.09–0.72). Although marginally significant, it is worth noting that cough (p = 0.051) was less likely to present in the 2nd tertile rather than the 3rd tertile (Table 3).
Table 3
Predicting timing of clinical onset of signs and symptoms for COVID-19

| Symptoms           | 1st Tertile [0–3] | 2nd Tertile [4–7] |
|--------------------|-------------------|-------------------|
|                    | RRR (95% CI)      | Std. Err          | p-value | RRR (95% CI)      | Std. Err | p-value |
| Sex                |                   |                   |         |                   |         |
| Male               | 1.00              | .                 | .       | 1.00              | .       | .       |
| Female             | 0.91 (0.46–1.81)  | 0.319             | 0.809   | 0.89 (0.43–1.82)  | 0.326   | 0.761   |
| Age                |                   |                   |         |                   |         |
| 19 Below           | 1.00              | .                 | .       | 1.00              | .       | .       |
| 20–29              | 0.21(0.05–0.87)   | 0.153             | 0.032   | 0.20(0.04–0.83)   | 0.146   | 0.027   |
| 30–39              | 0.20(0.05–0.81)   | 0.145             | 0.025   | 0.18(0.04–0.72)   | 0.129   | 0.015   |
| 40–49              | 0.25(0.05–1.16)   | 0.198             | 0.078   | 0.20(0.04–0.92)   | 0.156   | 0.039   |
| 50++               | 0.13(0.02–0.61)   | 0.102             | 0.010   | 0.09(0.01–0.47)   | 0.077   | 0.004   |
| Fever              |                   |                   |         |                   |         |
| No                 | 1.00              | .                 | .       | 1.00              | .       | .       |
| Yes                | 0.92(0.48–1.78)   | 0.309             | 0.824   | 0.55(0.26–1.15)   | 0.206   | 0.114   |
| Cough              |                   |                   |         |                   |         |
| No                 | 1.00              | .                 | .       | 1.00              | .       | .       |
| Yes                | 0.62(0.34–1.15)   | 0.194             | 0.133   | 0.53(0.28–1.00)   | 0.172   | 0.051   |
| Sore throat        |                   |                   |         |                   |         |
| No                 | 1.00              | .                 | .       | 1.00              | .       | .       |
| Yes                | 1.32 (0.63–2.77)  | 0.498             | 0.453   | 0.70 (0.30–1.65)  | 0.306   | 0.425   |
| Shortness of breath|                   |                   |         |                   |         |
| No                 | 1.00              | .                 | .       | 1.00              | .       | .       |
| Yes                | 1.23 (0.44–3.47)  | 0.652             | 0.683   | 1.59(0.51–4.90)   | 0.913   | 0.414   |
| Headache           |                   |                   |         |                   |         |
| No                 | 1.00              | .                 | .       | 1.00              | .       | .       |
| Yes                | 0.50 (0.24–1.04)  | 0.187             | 0.065   | 0.78(0.37–1.62)   | 0.291   | 0.508   |
| Chest pain         |                   |                   |         |                   |         |
| No                 | 1.00              | .                 | .       | 1.00              | .       | .       |
| Yes                | 0.43 (0.18–1.00)  | 0.186             | 0.052   | 0.26 (0.09–0.72)  | 0.135   | 0.009   |
| Running Nose       |                   |                   |         |                   |         |

Note. Estimation is based on MLR, where n = 290, LR Chi2 = 42.3, p-value = 0.0101; base category is 3rd Tertile denoting at-least 7 days after laboratory confirmation for COVID-19; RRR denotes the Relative Risk Ratio
| Symptoms | 1st Tertile [0–3] | 2nd Tertile [4–7] |
|---------|-----------------|-----------------|
|         | RRR (95% CI)    | Std. Err | p-value | RRR (95% CI)    | Std. Err | p-value |
| No      | 1.00            | .         | .       | 1.00            | .         | .       |
| Yes     | 0.45 (0.24–0.84)| 0.142     | 0.012   | 0.64 (0.33–1.21)| 0.209     | 0.176   |
| _cons   | 12.46(2.95–52.50)| 9.14      | 0.001   | 13.36 (3.15–56.53)| 9.83      | 0.000   |

Note. Estimation is based on MLR, where n = 290, LR Chi2 = 42.3, p-value = 0.0101; base category is 3rd Tertile denoting at-least 7 days after laboratory confirmation for COVID-19; RRR denotes the Relative Risk Ratio

Discussion

The common symptoms at onset of illness in the findings were cough, running nose, fever, headache and sore throat; while the less common symptoms were vomiting, diarrhea, nausea as well as abdominal pain and joint pain. The highest proportion of cases (37.5%) presented symptom in the 1st tertile denoting onset within three days after laboratory confirmation for SARS-CoV-2; while the rest had symptoms either in the 2nd (31.4%) or 3rd tertile (31.4%) denoting 4–6 days and at-least 7 days after exposure, respectively. Running nose and chest pain were less likely to occur in the 1st tertile (RRR = 0.45, 95% CI 0.24–0.84) and 2nd tertile (RRR = 0.64, 95% CI 0.09–0.72) rather than in the 3rd tertile. Cases aged 20–29, 30–39, 40–49 and above 49 were less likely to have symptoms in the 1st and 2nd tertile compared to those aged below 20 years (p < 0.05).

The clinical features of patients infected with the 2019 novel coronavirus in Uganda are to a greater extent similar with recent findings of patients diagnosed with the virus in Wuhan, China [15]. The patients in Wuhan, China presented common symptoms at onset of illness to be fever, cough, and myalgia or fatigue while the less common symptoms were sputum production, headache, haemoptysis, and diarrhoea. Both studies present cough and fever as common symptoms at onset of illness and diarrhea as less common symptom. However, headache was established as one of the common symptoms at onset among patients in Uganda while it was established among the less common symptoms in Wuhan, China. Further, muscle and joint pain were established as less common symptoms at onset in Uganda while these were established among the common symptoms in Wuhan, China. This evidence shows both similarities and differences in epidemiological characterization of cases exposed to COVID-19 in Uganda and elsewhere.

Running nose and chest pain were less likely to occur in the 1st tertile and 2nd tertile rather than in the 3rd tertile. The chest pain is considered as one of the emergency warning signs and symptoms for COVID-19 including trouble breathing, persistent pain or pressure in the chest, confusion or inability to arouse the person, or bluish lips or face (12,13). It is highly unlikely that these signs or symptoms will present at the initial stages of the illness. Therefore, evidence of these implies that COVID-19 symptoms have worsened after several days of the illness; which is more likely in the latter stages of the incubation period. It’s an indication of disease progression from mild to severe form of COVID-19 illness.

It is evident in the findings that symptom onset in the 1st and 2nd tertile was less likely among cases aged at-least 20 years compared to the younger ones. In other words, the cases aged below 20 years were more likely to have symptom onset earlier after exposure to COVID-19 compared to their older counterparts. Though the younger age group onset of symptoms occurred earlier than the older age-groups, the symptoms were indications of mild disease rather than severe illness. Our findings seems to concur with evidence suggesting that older people (that is people over 60 years old) are at a higher risk of getting severe COVID-19 disease(13,14) In particular, the literature suggests that the
risk of severe disease gradually increases with age starting from around 40 years. We cannot be able to substantiate the literature since the cases in our study are predominantly a young population (median age is 33 years, IQR = 26–41). The fact that symptom onset in the 1st and 2nd tertile was less likely among cases aged at-least 20 years, one would not expect onset and severe disease to occur at the same time in the 3rd tertile. Therefore, our findings present the young population (aged below 20 years) as a vulnerable group that needs to be given attention. More so, they can be a source of community spread of infection and a risk to the older generation.

Our study showed no significant variations in timing of onset for the following symptoms: fever, sore throat, shortness of breath, cough and headache ($p > 0.05$). Although marginally significant, it is worth noting that headache ($p = 0.065$) and chest pain ($p = 0.052$) were less likely to present in the 1st tertile rather than the 3rd tertile. Likewise, cough ($p = 0.051$) was less likely to present in the 2nd tertile rather than the 3rd tertile. Chest pain is considered as one of the emergency warning signs and symptoms for COVID-19, which is unlikely to present at the initial stages of the illness(13,14). On the other hand, we cannot substantiate the presentation of headache and cough in the 3rd tertile since these have not been identified among the emergency warning signs and symptoms for COVID-19 that would possibly present in the latter stages of the illness.

Studies have shown that majority of confirmed cases for the SARS-CoV-2 infection were males (14,19–21). Nevertheless, we found no significant variation in timing of symptom onset by sex ($p > 0.05$). This evidence seems contrary to studies in China, South Korea, United States, and Italy that have reported an association between the sex of COVID-19 patients and fatality rates as well as critically-ill status(13–16,19–21). For example, cases with fatality rates were higher in male patients than females (13–15), less female patients needed intensive care or died compared to male patients [19]; women were significantly less prone to develop the severe form of the disease (19); some symptoms were experienced significantly more by male than female, including cough and fever(20). In a study of sex differentials in COVID-19 patients, Maleki et al.(21) arguments for these variations include the following: women's immune cells activate more than men, women produce lower levels of interleukin-6 (IL-6) compared to men, which is associated with better longevity; different levels of Angiotensin Converting Enzyme-2 (ACE2) in men and women, the effects of testosterone on ACE2 levels, and the fact that the ACE2 gene is located on the X-chromosome. In citing Fagone et al. (22), Maleki et al. (21) writes: "in age group of 40 to 60 years, the transcriptomic characteristics of female lung tissue has more similarities to COVID-19-induced characteristics compared to male tissue. A possible explanation of the lower incidence of COVID-19 in female patients could be the lower threshold of acute immune response to COVID-19 in men when compared to women".

**Conclusion**

Studies have shown that the time between exposure to the virus and symptom onset can be up to 14 days. Our study characterized the period within three groups namely 1st tertile, 2nd tertile and 3rd tertile. Running nose and chest pain were less likely to occur in the 1st and 2nd tertile, denoting 0–3 days and 4–6 days after laboratory-confirmed for COVID-19 infection, respectively. Cases aged 20 year and above were less likely to present symptoms in the 1st and 2nd tertile. Our study provides empirical evidence for epidemiological characterization of cases by signs and symptoms along the incubation period. This complements the current proposals for the length of active monitoring of persons potentially exposed to SARS-CoV-2. It is important to note that publicly reported cases may over represent severe cases, the incubation period for which may differ from that of mild cases. In addition our study does not assess any co-morbidities which may potentially influence timing of symptom onset. Therefore, our findings should be interpreted in light of this consideration.

**Abbreviations**
Declarations

Ethics approval and consent to participate

The data collection was a response to a public health emergency in Uganda. Thus, the Ministry of Health - which is responsible for the overall response against COVID-19 in the country - ruled that no formal ethics approval was required in this particular case.

Data availability statement

Participant data without names and identifiers will be made available after approval from the corresponding author and Uganda National Institute of Public Health, Ministry of Health, Kampala, Uganda.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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Authors' contributions

ARA, LB, CB, BBM, RW, NK, DK and HBK designed the study. ARA collated the data under the Uganda National Institute of Public Health, Ministry of Health. RW and NK analyzed the data. ARA, LB, CB, BBM, RW, NK, DK and HBK contributed to interpreting the results. ARA, RW, NK and HK wrote the manuscript. ARA, LB, CB, BBM, RW, NK, DK and HBK revised the manuscript. All authors read and approved the final manuscript.

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**Figures**

*Clinical Onset of 1st Symptoms*

**Figure 1**
Figure 2

Timing of onset of first symptom(s) for COVID-19