

Journal Pre-proof

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PII: S1201-9712(21)00255-1

DOI: <https://doi.org/10.1016/j.ijid.2021.03.037>

Reference: IJID 5239

To appear in: *International Journal of Infectious Diseases*

Received Date: 3 February 2021

Revised Date: 27 February 2021

Accepted Date: 10 March 2021

Please cite this article as: Abraha HE, Gessesse Z, Gebrecherkos T, Kebede Y, Weldegiorgis AW, Tequare MH, Welderifael AL, Zenebe D, Gebremariam AG, Dawit TC, Gebremedhin DW, de Wit TR, Wolday D, Clinical Features and Risk Factors Associated with Morbidity and Mortality Among COVID-19 Patients in Northern Ethiopia, *International Journal of Infectious Diseases* (2021), doi: <https://doi.org/10.1016/j.ijid.2021.03.037>

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Clinical Features and Risk Factors Associated with Morbidity and Mortality Among COVID-19 Patients in Northern Ethiopia

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Highlights

- Compulsory quarantine of all Ethiopia patients with confirmed SARS-CoV-2 infection allowed to better analyze magnitude of asymptomatic infection.
- Comprehensive clinical features and representative morbidity and mortality outcomes of COVID-19 in Sub-Saharan Africa setting.
- A significant proportion of patients with asymptomatic and pre-symptomatic clinical presentations.
- Co-infection with HIV is a significant risk factor for developing severe COVID-19.

ABSTRACT

Objective: To describe clinical features and assess determinants of severity and in-hospital mortality of COVID-19 patients from unique setting in Ethiopia.

Methods: Consecutive patients admitted to COVID-19 quarantine and isolation center were included. We analyzed proportions of clinical spectrum of COVID-19, factors associated with risk of severe COVID-19 and in-hospital mortality.

Results: Of 2617 patients, three-quarter of the quarantined (N=1935; 74%) appeared asymptomatic, and only 114 (4.4%) presented with severe COVID-19. Common characteristics among the 682 symptomatics were cough (N= 354; 50.6%), myalgia (N=212; 31.1%), head ache (N=196; 28.7%), fever (N=161; 23.6%), dyspnea (N=111; 16.3%), anosmia and/or dysgeusia (N=90; 13.2%), sore throat (N=87; 12.8%) and chest pain (N=77; 11.3%). Factors associated with severe COVID-19 were older age [adjusted relative risk (aRR) 1.78, 95% CI 1.61 to 1.97; $p<0.0001$], diabetes (aRR 2.00, 95% CI 1.20 to 3.32; $p=0.007$), cardiovascular diseases (aRR 2.53, 95% CI 1.53 to 4.17; $p<0.0001$), malignancy (aRR 4.57, 95% CI 1.62 to 12.87; $p=0.004$),

surgery/trauma (aRR 23.98, 95% CI 10.35 to 55.57; $p<0.0001$), and infection with HIV-1 (aRR 4.24, 95% CI 1.55 to 11.61; $p=0.005$). Factors associated with risk of in-hospital mortality included older age (aRR 2.37, 95% CI 1.90 to 2.95; $p<0.001$), malignancy (aRR 6.73, 95% CI 1.50 to 30.16; $p=0.013$) and surgery/trauma (aRR 59.52, 95% CI 12.90 to 274.68; $p<0.0001$).

Conclusions: Significant proportion of SARS-CoV-2 infection were asymptomatic and key comorbid conditions increased risk of COVID-19 severity and in-hospital mortality. These findings could help in the design of appropriate management of patients.

Key words: COVID-19, Africa, comorbidities, clinical features, Ethiopia, SARS-CoV-2, mortality

1. Introduction

A novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), that emerged in Wuhan, China, has resulted in unprecedented global pandemic of respiratory illness, termed coronavirus disease 2019 (COVID-19) (Huang et al., 2020, WMHC 2020, Zhu et al., 2020). As of 3 February 2021, more than 104 million cases of COVID-19 and 2.26 million deaths were reported worldwide (WHO, 2021). In Ethiopia, the first case was reported on March 13, 2020; and as of February 3, 2021, a total of 138,861 cases have been identified with 2,116 (1.5%) related deaths (JHU, 2021).

Earlier reports from China demonstrated that most patients with SARS-CoV-2 infection develop only asymptomatic or mild illness, approximately 14% develop severe disease that requires

hospitalization and oxygen support, and 5% require admission to an intensive care unit (Huang et al., 2020; WMHC 2020; Zhu et al., 2020). In severe cases, COVID-19 can be complicated by acute respiratory distress syndrome (ARDS), sepsis and septic shock, multi-organ failure, including acute kidney injury and cardiac injury (Cummings et al., 2020; Grasselli et al., 2020; Huang et al., 2020; Richardson et al., 2020; WMHC 2020; Wu et al., 2020; Zhu et al., 2020). The exact magnitude of asymptomatic infection remains unknown though estimated to be between 18% and 80% (Gandhi et al., 2020; Nikolai et al., 2020).

Most of clinical COVID-19 reports from high-income countries (HICs) are derived from symptomatic patients admitted to hospitals. In HICs, older age and underlying comorbidities due to non-communicable diseases (NCDs) such as hypertension, cardiovascular diseases and diabetes, were reported as risk factors for disease severity and death (Cummings et al., 2020; Grasselli et al., 2020; Richardson et al., 2020; Wu et al., 2020). However, in the setting of Sub-Saharan Africa (SSA), there is much less known information on COVID-19 symptomatology (Abayomi et al., 2020; Elimian et al., 2020; Kirenga et al., 2020; Nachege et al., 2020). An emerging literature is reporting significantly less COVID-19 related morbidity and mortality in SSA (Diop et al., 2020; Fonte et al., 2020; Mbow et al., 2020; Njenga et al., 2020). There are different hypotheses reported, including 20-year lower average age of SSA population, general underreporting of (causes of) mortality in SSA, significantly reduced COVID-19 testing coverage, different genetic backgrounds, different immune activation status and potential protection by helminth infections, cross-protection due to non-pathogenic coronaviruses (Gutman et al., 2020; Hays et al., 2020; Margolin et al., 2020; Mbow et al., 2020). In LMICs, communicable diseases, such as HIV-1, tuberculosis, malaria and other neglected infectious disease, are highly

prevalent (Gutman et al., 2020; Hays et al., 2020). Moreover, NCDs are being identified with increased frequency in SSA (Gutman et al., 2020).

The objective of this study was, therefore, to describe the clinical features, associated risk factors, and morbidity and mortality among patients with COVID-19 in Ethiopia.

2. Methods

Study design and participants

In this retrospective cohort study, we analyzed a consecutive series of COVID-19 patients admitted to Kuyha COVID-19 Isolation and Treatment Center, Mekelle University College of Health Sciences, Mekelle City, Tigray State, Northern Ethiopia. Following the declaration by the WHO that COVID-19 became pandemic, the Ethiopian Ministry of Health implemented a mass screening of all travelers, people who had come in contact with COVID-19 patients as well as those from high risk settings (e.g. health-care workers). PCR-confirmed COVID-19 cases between May 10 and October 16, 2020 were included. In this unique setting, all cases were either quarantined for 10 to 14 days, or admitted to hospital in Kuyha, depending on their clinical presentation. After this time, management guideline was changed and only those with symptoms were admitted.

Sociodemographic, clinical data and laboratory data were collected using standardized Case Record Forms (CRFs) adapted from the International Severe Acute Respiratory and Emerging Infection Consortium's (ISARIC, 2020). Patient's clinical status was stratified following WHO criteria as asymptomatic, mild/moderate, severe (with dyspnea, respiratory rate ≥ 30 breaths per minute, O_2 saturation $\leq 93\%$, lung infiltrates $\geq 50\%$ of the lung fields within 24-48 hours),

and critical (with respiratory failure, septic shock, and/or multiple organ failure) (WHO, 2020). For this study, asymptomatic and mild/moderate cases were considered as non-severe cases and both severe and critical were considered as severe cases. All data were then entered onto electronic medical records.

Statistical Analysis

Baseline characteristics for continuous variables were expressed as median with inter-quartile range (IQR), and for categorical variables as counts and percentages. For categorical variables, comparisons were performed using χ^2 test, or Fisher's exact test whenever any expected cell count was < 5 . Continuous variables were compared by Mann-Whitney U or Kruskal-Wallis tests as appropriate.

Factors associated with severe COVID-19 clinical presentation and in-hospital mortality were analyzed using Poisson regression analyses. Using univariate analysis, we initially analyzed the relative risk (RR) of severe disease or in-hospital mortality with respect to baseline demographic, clinical characteristics and comorbid conditions. Then a multivariate regression analyses [adjusted relative risk (aRR)] were calculated (with backward stepwise elimination) by including all variables that were $p < 0.10$ by univariate analysis. A two-sided $p < 0.05$ was considered statistically significant. Data were analyzed using STATA (Statistical package v. 15.0, StataCorp, Texas, USA).

3. Results

Characteristics of study participants

During the study period, 61,599 individuals were tested for SARS-CoV-2. A total of 2,617 (4.3%) patients tested positive by RT-PCR for SARS-CoV-2 were included in the study (Figure 1, Table 1). The majority of our study population were male (63.3%), and among the 960 females enrolled, 27 (2.8%) were pregnant. The median age of the cohort was 29 (IQR 24–38) years, the majority (66.9%) being in the age range 20 to 39 years. Whereas the proportion of children below 20 years of age was 9.2% (n=242), with a median age of 17 (IQR 14–18) years, those aged ≤ 10 years constituted only 1.1%, with a median age of 4 (IQR 1–7) years. The proportion of those aged ≥ 60 years was only 5.7%, with a median age of 67 (IQR 62–75) years. Many patients reported a history of recent travel (57.9%) and very few (4.6) reported contact history with a known confirmed case of COVID-19.

Most notably, 92.6% the cohort population were asymptomatic at the time of diagnosis (Figure 1). The remaining had either mild/moderately symptomatic (4.7%), or presented with severe disease (2.7%). During quarantine, 488 patients subsequently progressed from asymptomatic to mild/moderate clinical presentation, while a total of 43 cases with an initial mild/moderate clinical presentation developed severe/critical disease conditions. Overall, almost a quarter of the cohort (74%) remained as asymptomatic during the entire quarantine period (median 12 days, IQR: 10-14 days) while 21.7% had mild/moderate and only 4.4% had severe/critical disease. Of the 114 severe cases, only 15 (13.2%) required mechanical ventilation. Patients with severe clinical presentation were predominantly male and older than non-severe patients (Table 1). Health care workers comprised 8.8% of the infected population, of which the majority presented with asymptomatic or mild/moderate symptoms. Among COVID-19 patients who

presented with symptoms, the most common were cough (50.6%), myalgia (31.1%), head ache (28.7%), fever (23.6%), dyspnea (16.3%), anosmia and/or dysgeusia (13.2%), sore throat (12.8%) and chest pain (11.3%) (Table 2). Diarrhea (3.5%) and hemoptysis (1.9%) were reported with lower frequencies. However, among those with severe COVID-19, the most common symptoms included cough (96.5%), dyspnea (66.7%), myalgia (55.3%), head ache (32.5%), fever (29.8%), chest pain (18.4%), and anosmia and/or dysgeusia (14.0%).

Comorbidities and other conditions

A total of 285 (10.9%) COVID-19 patients had at least one comorbidity, of which 30 (10.5%) had ≥ 2 comorbid conditions (Table 3). NCDs comprised the majority (87.7%), with diabetes (3.1%), cardio vascular diseases, including hypertension (3.1%), and chronic obstructive lung diseases, including asthma (2.8%) being the most frequent. Of all female COVID-19 patients, 2.8% were pregnant. Overall, comorbidity conditions were significantly higher among those who presented with severe disease (53.5%) when compared with the proportion of comorbidity in those with non-severe clinical presentation (9.0%) ($P < 0.0001$). In addition, despite low frequencies, communicable diseases, in particular HIV was reported more frequently among severe (3.5%) than in non-severe (0.8%) COVID-19 patients ($P = 0.003$). Of the 24 HIV infected COVID-19 patients, 21 (~88%) were already on antiretroviral therapy while only 3 were newly diagnosed.

Factors associated with severe COVID-19 and in-hospital mortality

Of the 2617 COVID-19 cases admitted, only 114 (4.4%) patients presented with a severe form of the disease. Risk factors associated with severe COVID-19 clinical presentation are summarized in Table 4. On multivariate analysis, the risk factors significantly associated with severe COVID-

19 were older age (aRR 1.78, 95% CI 1.61 to 1.97; $p < 0.0001$) and having any comorbid condition (aRR 3.56, 95% CI 2.36 to 5.38; $p < 0.0001$), in particular NCDs (aRR 3.64, 95% CI 2.39 to 5.54; $p < 0.0001$). Of the NCDs, diabetes (aRR 2.00, 95% CI 1.20 to 3.32; $p = 0.007$), cardiovascular diseases (aRR 2.53, 95% CI 1.53 to 4.17; $p < 0.0001$), malignancy (aRR 4.57, 95% CI 1.62 to 12.87; $p = 0.004$) and surgery/trauma (aRR 23.98, 95% CI 10.35 to 55.57; $p < 0.0001$) were all associated with increased risk of severe COVID-19. Of all communicable diseases, HIV-1 co-infection was the only associated risk for severe COVID-19 (aRR 4.24, 95% CI 1.55 to 11.61; $p = 0.005$).

Of all our patients in the cohort, only 20/2617 (0.8%) died during in-hospital admission. Five (0.2%) patients were either transferred-out to other facilities or lost to follow-up. Overall, 2592 (99.9%) of the admitted patients recovered and were discharged. None of the children aged below 20 years died; only 2 deaths (10%) were in the age group 20 to 39 years, 4 (20%) were among those aged 40 to 59 years, and the remaining majority ($n = 14$, 70%) were ≥ 60 years old. On multivariate analysis, the factors significantly associated with increased risk of in-hospital mortality were older age (aRR 2.37, 95% CI 1.90 to 2.95; $p < 0.001$), malignancy (aRR 6.73, 95% CI 1.50 to 30.16; $p = 0.013$) and surgery/trauma (aRR 59.52, 95% CI 12.90 to 274.68; $p < 0.0001$).

4. Discussion

To the best of our knowledge, the current study is one of the first large cohort studies undertaken in SSA on a relatively representative population of SARS-CoV-2 infection. This was possible due to the unique setting of compulsory quarantine measures for all who tested SARS-CoV-2 positive as per the national guidelines. The true proportions of asymptomatic SARS-CoV-

2 infected patients is not known exactly (Gandhi et al., 2020; Nikolai et al., 2020). In our study, we noted high proportion (74%) of asymptomatic patients. The finding is somewhat similar to a recent report from Addis Ababa, the epicenter of SARS-COV-2 infection in Ethiopia, where the investigators reported 78% of asymptomatic cases (Abraham et al., 2020). Moreover, the findings are consistent with previous reports showing high proportions of asymptomatic SARS-CoV-2 carriers, ranging from 66% to 88% (Baggett et al., 2020; Barrett et al., 2020; Ing et al., 2020; Lytras et al., 2020), but higher than those reported from Nigeria, Uganda, the Middle East, Europe or United States, ranging from 45% to 58% (Abayomi et al., 2020; Almazeedi et al., 2020; Kirenga et al., 2020; Mizumoto et al., 2020; Moriarty et al., 2020). The implications of high proportions of asymptomatics for the spread of the pandemic in SSA remains to be determined. Nonetheless, it has been suggested that a high proportion of asymptomatic (or pre-symptomatic) infections fuel the pandemic through super-spreading events (Gandhi et al., 2020; Nikolai et al., 2020). Tracking and tracing, super-spreaders and their contacts and subsequent isolation/quarantine are a cornerstone of interrupting the transmission cycle of the pandemic. This is particularly challenging when super-spreaders are not having COVID-19 symptoms. It has been reported that asymptomatics transmit with 42% lower relative risk than symptomatics, with an unknown proportion of super-spreaders amongst asymptomatics (Buitrago-Garcia et al., 2020)

One of the challenges with respect to describing the overall clinical spectrum of COVID-19 in a particular geographical setting is that a significant proportion of the patients do progress from one status of clinical presentation to another. Indeed, the real magnitude of the proportion of patients initially diagnosed as asymptomatic, but who become subsequently symptomatic (also

known as pre-symptomatic cases) is hardly known. This study provides more information on this topic. Earlier report from China in a small sample size showed that a significant proportion (14/24, ~60%) of infected patients were pre-symptomatic and showed COVID-19 symptoms after 1 to 3 weeks (Hu et al., 2020). Likewise, another report from Japan showed that 11/96 (11.5%) asymptomatic SARS-COV-2 infected patients transferred from the cruise ship *Diamond Princess* to a hospital developed clinical signs and symptoms after a median of 4 days after the first positive PCR test (Sakurai et al., 2020). In addition, a study from Kuwait demonstrated 35/508 (6.9%) pre-symptomatic patients (Almazeedi et al., 2020). Interestingly, in our study, we identified a total of 488 (18.7%) asymptomatic patients who subsequently developed symptoms, indicating that these patients had been actually pre-symptomatic at the time of PCR testing. The observed wide difference in the range of pre-symptomatic cases seen in different countries might be related to the diverse clinical status of COVID-19 included in the various reports.

Our cohort comprised predominantly male patients, similar to previous studies (Abayomi et al., 2020; Almazeedi et al., 2020; Cummings et al., 2020; Gandhi et al., 2020; Grasselli et al., 2020; Nachega et al., 2020; Nikolai et al., 2020; Richardson et al., 2020; Wu et al., 2020). The median age in our cohort (29 years old) was lower compared to the studies reported from Africa that ranged between 33 and 46 years (Abayomi et al., 2020; Elimian et al., 2020; Kirenga et al., 2020; Nachega et al., 2020), the Middle East (41 years old) (Almazeedi et al., 2020), or China (49 years old) (Huang et al., 2020), and much lower than those reported from HICs (around 62 years old) (Cummings et al., 2020; Grasselli et al., 2020; Richardson et al., 2020;). Younger median age is an important factor explaining observed high proportion of asymptomatics. The median age in

our cohort among those with severe COVID-19 (60 years) is similar to other settings (Abayomi et al., 2020; Almazeedi et al., 2020; Cummings et al., 2020; Elimian et al., 2020; Gandhi et al., 2020; Grasselli et al., 2020; Kirenga et al., 2020; Nachega et al., 2020; Nikolai et al., 2020; Richardson et al., 2020; Wu et al., 2020). The proportion of children below 20 years of age in our cohort was 9.1%, and was higher than the one reported from Democratic Republic of Congo (DRC) or Nigeria (Abayomi et al., 2020; Nachega et al., 2020), but lower than the one reported from another study from Nigeria and Uganda (Elimian et al., 2020; Kirenga et al., 2020).

Typically, SARS-CoV-2 infection, in the majority of children, manifests as asymptomatic or mild disease (Wald et al., 2020). Hence, the higher proportion of children noted in our study and other African countries (Elimian et al., 2020; Kirenga et al., 2020) might be related to the inclusion of all COVID-19 patients that included a significant proportion of asymptomatic cases. The proportion of patients aged ≥ 60 years in our cohort was low (5.7%) when compared to those reported from DRC or Nigeria (Abayomi et al., 2020; Nachega et al., 2020).

Among the cohort participants who were symptomatic, the most frequent symptoms noted at presentation were cough (50.6%), myalgia (31.1%), head ache (28.7%), fever (23.6%), dyspnea (16.3%), anosmia and/or dysgeusia (13.2%), sore throat (12.8%) and chest pain (11.3%). cough (96.5%), dyspnea (66.7%), myalgia (55.3%), head ache (32.5%), fever (29.8%), chest pain (18.4%), and anosmia and/or dysgeusia (14.0%) were the most common symptoms reported among those who developed severe form of COVID-19. Anosmia and dysgeusia was less frequent in non-severe than in severe COVID-19 patients in our cohort. This was somewhat similar to the report from Nigeria (Abayomi et al., 2020), or South Africa (Parker et al., 2020), but different from the one from DRC where they showed none of their study participant

showed such symptoms (Nachega et al., 2020). Diarrhea was present in few (3.5%) patients, that was somewhat similar to the one reported from Nigeria or Uganda (Abayomi et al., 2020; Kirenga et al., 2020).

The proportion of severe COVID-19 in our cohort was low (4.4%) when compared to the study from DRC (Nachega et al., 2020), though somewhat similar to those reported from Uganda, Nigeria and Kuwait (Abayomi et al., 2020; Almazeedi et al., 2020; Elimian et al., 2020; Kirenga et al., 2020). However, severe cases of COVID-19 requiring hospitalization ranges between 10% and 20% in settings in HICs (Gary et al., 2020; Kimbal et al., 2020; Mizumoto et al., 2020; Huang et al., 2020; WMHC 2020; Zhu et al., 2020). Consistent with previous reports (Abayomi et al., 2020; Almazeedi et al., 2020; Cummings et al., 2020; Gandhi et al., 2020; Grasselli et al., 2020; Nachega et al., 2020; Nikolai et al., 2020; Richardson et al., 2020; Wu et al., 2020), our findings showed that a significant proportion of patients in our cohort have preexisting comorbid conditions leading to severe COVID-19 and mortality. Overall, NCDs were more prevalent than communicable diseases. The most common NCDs among those with severe COVID-19 were cardiovascular diseases, including hypertension (24.6%), diabetes (18.4%) and chronic obstructive lung diseases, including asthma (5.3%). The overall proportion of such comorbid conditions in both non-severe and severe COVID-19 patients in our cohort was lower than those reported previously, both in HIC (Cummings et al., 2020; Grasselli et al., 2020; Richardson et al., 2020; Wu et al., 2020) as well as LMICs (Abayomi et al., 2020; Nachega et al., 2020; Parker et al., 2020). In addition, albeit small in number, we found that co-infection with HIV-1 was an independent and significant risk factor for COVID-19 severity. In our study, we did not find any association between tuberculosis and COVID-19 severity, as well as both HIV and

tuberculosis did not contribute to in-hospital mortality. Our finding that HIV did not impact in-hospital mortality was similar to the study from DRC and South Africa (Nachega et al., 2020; Parker et al., 2020). However, this was different when compared to another study from Western Cape Province in South Africa (Boulle et al., 2020), where both HIV and tuberculosis independently increased risk of COVID-19 mortality. Such differences might be attributed to the overall low proportion of mortality observed in our cohort or other African countries (Nachega et al., 2020; Parker et al., 2020), when compared to the cohort from Cape Town, South Africa (Boulle et al., 2020). In addition, we did not find any association between malaria and COVID-19 severity, however, the number of malaria cases were very small to draw firm conclusion. The proportion of health care workers (HCWs) infected with SARS-CoV-2 in our cohort was 8.8%, which was lower than the one reported from Nigeria which was 14.3% (Elimian et al., 2020). Whereas HCWs are at increased risk of developing severe disease (Rothan et al., 2020), there was no increased risk for severe COVID-19 or mortality noted in our cohort.

SSA has recorded a total of 3,614,270 cases and 92,472 deaths as of 3 February 2021, representing a CFR of 2.6% (WHO, 2021). The overall mortality rate among COVID-19 patients in our cohort was significantly lower (0.8%), and also lower than the national Ethiopian case fatality rate, estimated at 1.5% (JHU, 2021), when compared to the reports from DRC at 13.2% (Nachega et al., 2020), Nigeria at 9.2% (Elimian et al., 2020) or South Africa at 26.7% (Parker et al., 2020). The main reason for the observed lower mortality in our cohort compared to other SSA countries might be related to the inclusion of a significant proportion of asymptomatic cases in our cohort. In-hospital mortality rate among severe COVID-19 patients in our cohort is lower (28.6%) compared to the mortality rate among severe COVID-19 cases from DRC at 45%

(Nachega et al., 2020), or South Africa at 47.6% (parker et al., 2020). In addition, there was no death reported in the age group below 20 years in our cohort compared to 11.8% and 2.4% among those reported from DRC and Nigeria, respectively (Nachega et al., 2020; Elimian et al., 2020). Such differences might be attributed due to the more young age, lower prevalence of comorbid conditions along with predominantly asymptomatic or mild SARS-CoV-2 infections in our cohort. In addition, coinfection with parasites that are known to modulate immune response and reduce hyper inflammation associated with increased risk for severity in COVID-19 patients might play significant role (Hays et al., 2020). Prospective studies are underway in our setting to see whether coinfection with parasites mute COVID-19 severity.

Major strengths of this study includes the enrollment of all RT-PCR confirmed COVID-19 patients to a single center admitted for treatment and/or quarantine, irrespective of COVID-19 severity. Hence, the true proportion of patients with asymptomatic clinical presentation or severe cases can be determined. Another strength of the current study is the inclusion of larger sample size, as compared to previous studies from SSA. On the contrary, the current study has several shortcomings. First, missing data due to retrospective nature of the study design, precluding detailed analyses of factors that may impact risk for severity and in-hospital mortality. Second, incomplete data of key laboratory markers limit the power of risk factor association analyses. Third, the sample size of communicable diseases is too small to conclude that such diseases, in particular malaria and tuberculosis, do not influence COVID-19 severity. Fourth, due to the retrospective nature of this particular study, we were not able to measure the antibody seroconversion rate of those who remained symptomless. Finally, the study may

not be generalizable to the rest of SSA as setting for admission criteria is diverse between countries.

5. Conclusion

The current study is, to the best of our knowledge, one of the first comprehensive assessment of clinical spectrum of COVID-19 admitted to a single center for in SSA setting for treatment and/or quarantine. The study provided also information on the most relevant comorbid risks related to NCDs for severe COVID-19, that are similar to previous studies reported from HICs as well as LMICs (Abayomi et al., 2020; Elimian et al., 2020; Grasselli et al., 2020; Nachega et al., 2020; Richardson et al., 2020; Wu et al., 2020). More importantly, we provide evidence that HIV-1 coinfection, highly prevalent in SSA (70% of the global prevalence) (Margolin et al., 2020), is strongly associated with increased risk of COVID-19 severity. However, future cohort studies are needed to address the effect of other highly prevalent infections in SSA, including tuberculosis and malaria.

Funding

The project has received funding, in part, from the European and Developing Countries Clinical Trials Partnership (EDCTP) – European Union (Profile-Cov project, Grant #: RIA-2020EF-2095).

Ethical approval

The study protocol was reviewed and approved by the Health Research Ethics Review Committee (HRERC) of Mekelle University College of Health Sciences (#ERC 1822/2020). As the nature of the study was retrospective, individual study participant consent was not obtained

and approved by the ethics review committee. Nonetheless, all personal identifiers were de-linked from the original sources.

Conflict of interest

None.

Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

We thank all the staff of the Kuyha COVID-19 Isolation and Treatment Center, Mekelle University College of Health Sciences for their cooperation.

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Figure caption

Figure 1. Flow diagram of clinical spectrum of COVID-19.

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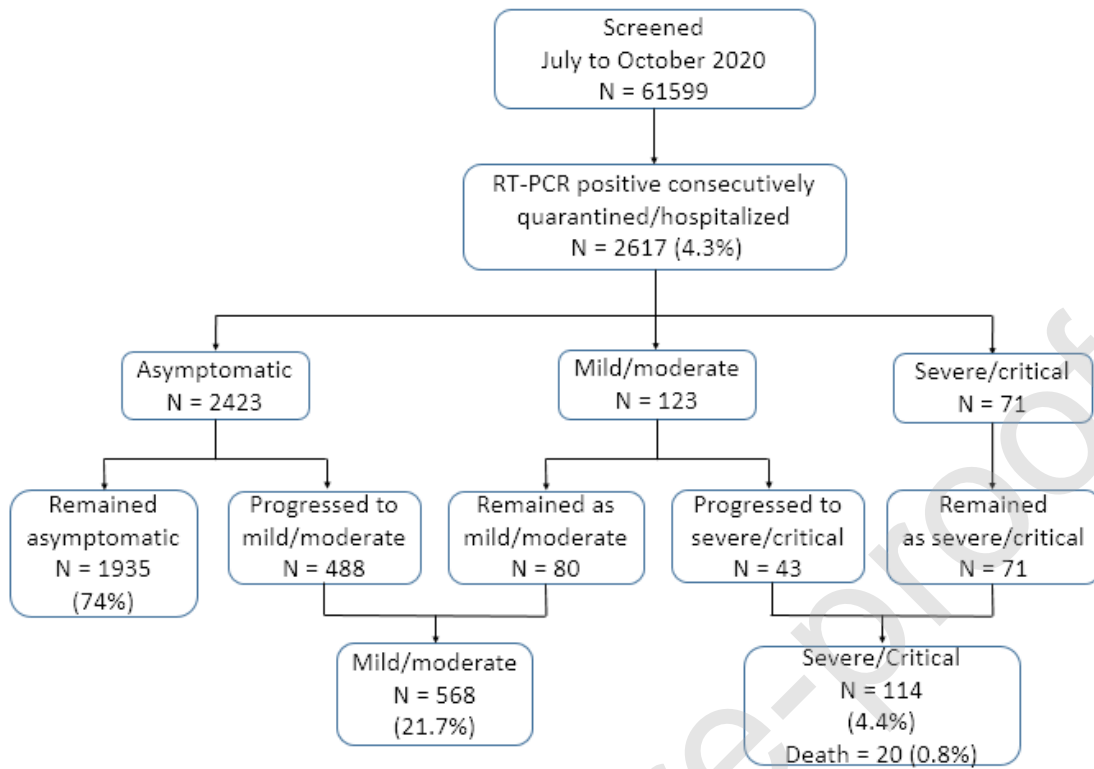


Figure 1. Flow diagram of clinical spectrum of COVID-19

Table 1. Baseline socio-demographic and clinical characteristics of COVID-19 patients in Northern Ethiopia

Characteristic	All patients N=2617	Non-severe patients (asymptomatic and mild/moderate) N= 2503	Severe patients (severe and critical) N= 114	P value
Socio-demographic features:				
Gender (male), N (%)	1657 (63.3)	1569 (62.7)	88 (77.2)	0.002
Age in years [median (IQR)]	29 (24–38)	29 (24–38)	55 (38–74)	<0.00001
Age group [years, N (%)]				
< 20	242 (9.2)	234 (9.4)	8 (7.0)	<0.0001
20 – 39	1752 (66.9)	1730 (69.1)	22 (19.3)	
40 – 59	475 (18.2)	443 (17.7)	32 (28.1)	
≥ 60	148 (5.7)	96 (3.8)	52 (45.6)	
Health care workers, N (%)	229 (8.8)	224 (9.0)	5 (4.4)	0.092
Urban residents, N (%)	698 (26.8)	669 (26.9)	29 (25.4)	0.392

History of travel, N (%)	1514 (57.9)	1409 (56.3)	105 (92.1)	<0.0001
History of contact with COVID-19 patient, N (%)	119 (4.6)	117 (4.8)	2 (1.8)	0.143
Clinical symptoms and signs:				
Fever, N (%)	161 (6.2)	127 (5.1)	34 (29.8)	<0.0001
Dyspnoea, N (%)	111 (4.2)	35 (1.4)	76 (66.7)	<0.0001
Cough (any type, N (%))	345 (13.2)	274 (11.0)	71 (62.3)	<0.0001
Non-productive cough	191 (7.3)	157 (6.3)	34 (29.8)	<0.0001
Productive cough	154 (5.9)	117 (4.7)	37 (32.5)	<0.0001
Hemoptysis, N (%)	13 (0.5)	10 (0.4)	3 (2.6)	0.001
Chest pain, N (%)	77 (2.9)	56 (2.2)	21 (18.4)	<0.0001
Sore throat, N (%)	87 (3.3)	74 (3.0)	13 (11.4)	<0.0001
Head ache, N (%)	196 (7.5)	159 (6.4)	37 (32.5)	<0.0001
Nasal congestion, N (%)	59 (2.3)	55 (2.2)	4 (3.5)	0.356
Anosmia and/or dysgeusia, N (%)	90 (3.4)	74 (3.0)	16 (14.0)	<0.0001
Diarrhoea, N (%)	24 (0.9)	20 (0.8)	4 (3.5)	0.003

Myalgia, N (%)	212 (8.1)	149 (6.0)	63 (55.3)	<0.0001
Temperature (median °C, IQR)	36.0 (36.0–36.7)	36.0 (36.0 – 36.7)	36.3 (36.0 – 36.7)	0.6756
Systolic blood pressure (median mmHg, IQR)	115 (108–125)	115 (109 – 125)	118 (110 – 125)	0.9616
Diastolic blood pressure (median mmHg, IQR)	75 (67 – 80)	75 (67 – 80)	76 (69 – 80)	0.2523
Respiratory rate (median breaths/minute, IQR)	21 (19 – 22)	21 (19 – 22)	22 (20 – 23)	0.1654
Heart rate (median beats/minute, IQR)	80 (74 – 88)	80 (73 – 88)	81 (74 – 90)	0.3292

Table 2. Comparison of socio-demographic and clinical characteristics of mild/moderate vs. severe COVID-19 patients in Northern Ethiopia

Characteristic	All symptomatic patients N=682	Mild/moderate N= 568	Severe (severe and critical) N= 114	P value
Socio-demographic features:				
Gender (male), N (%)	471 (69.1)	383 (67.4)	88 (77.2)	0.040
Age in years [median (IQR)]	32 (26-46)	30 (25-40)	55 (38–74)	<0.00001
Age group [years, N (%)]				
< 20	36 (5.3)	28 (4.9)	8 (7.0)	<0.0001
20 – 39	418 (61.3)	396 (69.7)	22 (19.3)	
40 – 59	139 (20.4)	107 (18.9)	32 (28.1)	
≥ 60	89 (13.0)	37 (6.5)	52 (45.6)	
Health care workers, N (%)	110 (16.1)	105 (18.5)	5 (4.4)	<0.0001

Urban residents, N (%)			29 (25.4)	0.107
History of travel, N (%)	493 (74.3)	396 (71.0)	97 (91.5)	<0.0001
History of contact with COVID-19 patient, N (%)	26 (4.1)	24 (4.5)	2 (2.0)	0.231
Clinical symptoms and signs:				
Fever, N (%)	161 (23.6)	127 (22.4)	34 (29.8)	0.087
Dyspnoea, N (%)	111 (16.3)	35 (6.2)	76 (66.7)	<0.0001
Cough (any type, N (%))	354 (50.6)	274 (48.2)	110 (96.5)	<0.0001
Non-productive cough	191 (28.0)	157 (27.6)	34 (29.8)	
				0.636
Productive cough	154 (22.6)	117 (20.6)	37 (32.5)	0.006
Hemoptysis, N (%)	13 (1.9)	10 (1.8)	3 (2.6)	0.535
Chest pain, N (%)	77 (11.3)	56 (9.9)	21 (18.4)	0.008
Sore throat, N (%)	87 (12.8)	74 (13.0)	13 (11.4)	0.635
Head ache, N (%)	196 (28.7)	159 (28.0)	37 (32.5)	0.337
Nasal congestion, N (%)	59 (8.7)	55 (9.7)	4 (3.5)	0.032

Anosmia and/or dysgeusia, N (%)	90 (13.2)	74 (13.0)	16 (14.0)	0.772
Diarrhoea, N (%)	24 (3.5)	20 (3.5)	4 (3.5)	0.995
Myalgia, N (%)	212 (31.1)	149 (26.2)	63 (55.3)	<0.0001
Temperature (median °C, IQR)	36.0 (36.0-36.7)	36.0 (36.0-36.7)	36.3 (36.0 – 36.7)	0.9616
Systolic blood pressure (median mmHg, IQR)	115 (108 – 125)	116 (110-125)	115 (105 – 1125)	0.7106
Diastolic blood pressure (median mmHg, IQR)	76 (69 – 76)	78 (70 – 81)	76 (69 – 80)	0.3882
Respiratory rate (median breaths/minute, IQR)	22 (20 – 22)	21 (18 – 22)	22 (20 – 23)	0.0047
Heart rate (median beats/minute, IQR)	81 (75 – 90)	82 (75 – 90)	81 (74 – 90)	0.6978

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Table 3. Comorbidities and underlying conditions among COVID-19 patients

Characteristic	All patients N=2617	Non-severe patients (asymptomatic and mild/moderate) N=2503	Severe patients (severe and critical) N=114	P value
Comorbidity (at least 1), N (%)	285 (10.9)	224 (9.0)	61 (53.5)	<0.0001
Comorbidity (≥ 2), N (%)	30 (1.2)	18 (0.7)	12 (10.5)	<0.0001
Non-communicable disease (NCD) comorbidities, N (%)	250 (9.6)	191 (7.6)	59 (51.8)	<0.0001
Communicable disease comorbidities, N (%)	39 (1.5)	35 (1.4)	4 (3.5)	0.069
Diabetes, N (%)	82 (3.1)	61 (2.4)	21 (18.4)	<0.0001
Cardiovascular disease, including hypertension, N (%)	82 (3.1)	54 (2.2)	28 (24.6)	<0.0001
Chronic obstructive lung diseases, including asthma, N (%)	72 (2.8)	66 (2.6)	6 (5.3)	0.094
Chronic liver disease, N (%)	5 (0.2)	5 (0.2)	0 (0.0)	0.633
Chronic kidney disease, N (%)	16 (0.6)	12 (0.5)	4 (3.5)	<0.0001
Malignancy, N (%)	9 (0.3)	5 (0.2)	4 (3.5)	<0.0001

Surgery/trauma, N (%)	13 (0.5)	7 (0.3)	6 (5.3)	<0.0001
Pregnancy among females, N (%)	27 (2.8)	26 (2.8)	1 (3.9)	0.747
HIV, N (%)	24 (0.9)	20 (0.8)	4 (3.5)	0.003
Tuberculosis, N (%)	8 (0.3)	8 (0.3)	0 (0.0)	0.545
Malaria, N (%)	9 (0.3)	8 (0.3)	1 (0.9)	0.320

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Table 4. Factors associated with severity among COVID-19 patients in Northern Ethiopia

Characteristic	Unadjusted Relative Risk (95% CI)	P-value	Adjusted Relative Risk (95% CI)	P-value
Gender (male vs. female)	1.96 (1.27 – 3.04)	0.003	1.33 (0.85 – 2.07)	0.212
Age (per 10 years older)	1.92 (1.76 – 2.09)	<0.0001	1.78 (1.61 – 1.97)	<0.0001
Health care workers (vs. others)	1.09 (0.72 – 1.63)	0.696		
Pregnancy	1.38 (0.19 – 10.20)	0.751		
Comorbidity (at least 1)*	9.42 (6.52 – 13.61)	<0.0001	3.56 (2.36 – 5.38)	<0.0001
Comorbidity (≥ 2)*	10.15 (5.58 – 18.45)	<0.0001	2.66 (1.44 – 4.89)	0.002
Non-communicable disease (NCD) comorbidities*	10.16 (7.03 – 14.67)	<0.0001	3.64 (2.39 – 5.54)	<0.0001
Communicable diseases comorbidities*	2.40 (0.89 – 6.52)	0.085		<0.0001
Diabetes**	6.98 (4.35 – 11.21)	<0.0001	2.00 (1.20 – 3.32)	0.007
Cardiovascular disease, including hypertension**	10.07 (6.57 – 15.42)	<0.0001	2.53 (1.53 – 4.17)	<0.0001

Chronic obstructive lung diseases, including asthma	1.96 (0.86 – 4.47)	0.108		
Chronic liver disease	2.06e-09 (0.00 – ..)	1.000		
Chronic kidney disease**	5.91 (2.18 – 16.03)	<0.0001	2.25 (0.81 – 6.24)	0.118
Malignancy**	10.54 (3.89 – 28.58)	<0.0001	4.57 (1.62 – 12.87)	0.004
Surgery/trauma**	11.13 (4.89 – 25.32)	<0.0001	23.98 (10.35 – 55.57)	<0.0001
HIV**	3.93 (1.45 – 10.65)	0.007	4.24 (1.55 – 11.61)	0.005
Tuberculosis	2.05e-09 (0.00 – ..)	1.000		
Malaria	2.56 (0.36 – 18.36)	0.348		

*Adjusted for gender and age

**Adjusted for gender, age, diabetes, cardiovascular diseases, malignancy and surgery/trauma

Table 5. Factors associated with in-hospital mortality among COVID-19 patients in Ethiopia

Characteristic	Unadjusted Relative Risk (95% CI)	P-value	Adjusted Relative Risk (95% CI)	P-value
Gender (male vs. female)	2.32 (0.78 – 6.93)	0.133	1.37 (0.45 – 4.18)	0.583
Age (per 10 years older)	2.33 (1.90 – 2.86)	<0.0001	2.37 (1.90 – 2.95)	<0.001
Health care workers (vs. others)	0.55 (0.07 – 4.10)	0.559		
Pregnancy	2.25e-09	1.000		
Comorbidity (at least 1)*	10.00 (4.14 – 24.13)	<0.0001	2.50 (0.98 – 6.37)	0.055
Comorbidity (≥ 2)*	21.56 (7.20 – 64.48)	<0.0001	4.86 (1.61 – 14.64)	0.005
Non-communicable disease (NCD) comorbidities*	11.57 (4.80 – 27.93)	<0.0001	2.73 (1.06 – 6.99)	0.037
Communicable diseases comorbidities*	2.29e-09	1.000		
Diabetes	7.73 (2.58 – 23.12)	<0.0001	2.50 (0.77 – 8.14)	0.129
Cardiovascular disease, including hypertension	7.73 (2.58 – 23.12)	<0.0001	1.36 (0.40 – 4.63)	0.623

Chronic obstructive lung diseases, including asthma	3.93 (0.91 – 16.93)	0.066		
Chronic liver disease	2.06e-09 (0.00 – ..)	1.000		
Chronic kidney disease	2.32e-09	1.000		
Malignancy**	32.20 (7.47 – 138.76)	<0.0001	6.73 (1.50 – 30.16)	0.013
Surgery/trauma**	22.26 (5.16 – 95.92)	<0.0001	59.52 (12.90 – 274.68)	<0.0001
HIV	231e-09	1.000		
Tuberculosis	2.05e-09 (0.00 – ..)	1.000		
Malaria	2.32e09	1.000		

*Adjusted for gender and age

**Adjusted for gender, age, diabetes, cardiovascular diseases, malignancy and surgery/trauma