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| Complete List of Authors: | Das, Pritimoy; International Centre for Diarrhoeal Disease Research Bangladesh<br>Akhtar, Zubair; International Centre for Diarrhoeal Disease Research Bangladesh<br>Mah-E-Muneer, Syeda ; International Centre for Diarrhoeal Disease Research Bangladesh<br>Islam, Md.; International Centre for Diarrhoeal Disease Research Bangladesh<br>Rahman, Mohammed; International Centre for Diarrhoeal Disease Research Bangladesh<br>Rahman, Mustafizur; International Centre for Diarrhoeal Disease Research Bangladesh<br>Rahman, Mahmudur; International Centre for Diarrhoeal Disease Research Bangladesh<br>Rahman , Mahbubur ; Institute of Epidemiology Disease Control and Research<br>Billah, Mallick; Institute of Epidemiology Disease Control and Research<br>Alamgir, A. S. M; Institute of Epidemiology Disease Control and Research<br>Flora, Meerjady Sabrina ; Institute of Epidemiology Disease Control and Research<br>Shirin, Tahmina; Institute of Epidemiology Disease Control and Research<br>Banu, Sayera; International Centre for Diarrhoeal Disease Research Bangladesh<br>Chowdhury, Fahmida; International Centre for Diarrhoeal Disease Research Bangladesh |



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# Establishing a sentinel surveillance system for the novel coronavirus disease 2019 (COVID-19) in a resource limited county: methods, system attributes and early findings

Pritimoy Das[1, †], Zubair Akhtar[1], Syeda Mah-E-Muneer[1], Md Ariful Islam[1], Mohammed Ziaur Rahman[1], Mustafizur Rahman[1], Mahmudur Rahman[1], Mahbubur Rahman[2], Mallick Masum Billah[2], ASM Alamgir[2], Meerjady Sabrina Flora[2], Tahmina Shirin[2], Sayera Banu[1], Fahmida Chowdhury[1]

[1]Infectious Diseases Division, International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b), Dhaka, Bangladesh
[2]Institute of Epidemiology, Disease Control and Research (IEDCR), Dhaka, Bangladesh

[†]Correspondence to Pritimoy Das; pritimoydas@gmail.com



## ABSTRACT

**Introduction:** icddr,b, and Institute of Epidemiology, Disease Control and Research (IEDCR), Government of Bangladesh, established a hospital-based surveillance platform for screening suspected COVID-19 patients to understand the COVID-19 situation in different regions where nearby testing facility (reverse transcription polymerase chain reaction, RT-PCR) was unavailable.

**Methods:** We conducted the surveillance at three secondary level public hospitals and one tertiary level private hospital in different regions, enrolled suspected COVID-19 patients with any of the symptoms within the last 7 days- fever, cough, sore throat, and respiratory distress. Surveillance staff recorded clinical and epidemiological data, collected and transported nasopharyngeal swabs to icddr,b, Dhaka for SARS-CoV-2 test using RT-PCR. Findings were reported to the authorities over email and the patients over short message service within 36 hours. Study staff followed up all patients after 30 days for the outcome of the illness over the telephone.

**Results:** From 10th June to 31st August 2020, COVID-19 was detected in 39% (922/2345) enrolled patients. It was more common in outpatients with a peak positivity in July (54%).

The median age of the confirmed COVID-19 cases was 38 years (IQR: 30-50), 71% were male, and 9% were healthcare workers. Among them, cough (67%) was the most common symptom, followed by fever (53%). Diabetic patients were more likely to get COVID-19 than non-diabetic (48% vs. 38%, p<0.05). The death rate among COVID-19 positive was 2.3% (21/922). Death was associated with age ≥ 60 years (OR:13.5; 95% CI: 5.4-33), shortness of breath (OR:14.4; 95% CI: 4.8-43), co-morbidity (OR:13.9; 95% CI: 3.2-60), smoking history (OR: 3.9, 95% CI: 1.5-9.8), attending to hospital in <2 days due to critical illness (OR: 5.4; 95% CI: 1.8-17) and hospital admission (OR:13.3; 95% CI: 5.3-33).

**Conclusion:** This surveillance strengthened government's capacity for rapid case detection, reporting, and quick containment efforts by taking data-driven effective strategy.

**Key words:** COVID-19, SARS-CoV-2, hospital based study, sentinel surveillance, Bangladesh

## Strengths and limitations of this study

- For the first time in the country, in collaboration with a government public health institution and an international research organization, we implemented a sentinel surveillance for COVID-19 in resource-constrained settings.
- This is a multicentre study with representative hospitals included from almost all major administrative regions of Bangladesh to ensure spatial distribution.
- More COVID-19 deaths were captured by the unique 30 days follow-up strategy compared to recorded in-hospital deaths (72% vs. 28%).
- We were unable to get data from the COVID-19 patients who did not go to the hospitals but remained in the community, thus community burden was not estimated.
- The true prevalence of COVID-19 patients could be higher than reported in our study as we did not screen any asymptomatic patients.

## Introduction

Starting from its inception at Wuhan, Hubei Province, China, the novel coronavirus named severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has spread across the world within a few months, causing Coronavirus Disease 2019 (COVID-19)[1]. Globally, 129,651,305 cases and 2.8 million deaths were recorded till 31th March 2021[2]. This virus manifests various clinical characteristics, from asymptomatic infection to severe pneumonia, vasculitis, and death[3–6]. It was declared a public health emergency of international concern (PHEIC) by the world health organization (WHO) in 30th January 2020 and subsequently a pandemic on 11th March 2020[7]. During that early stage of this coronavirus disease, there was uncertainty and variation regarding the epidemiological, clinical, and virological characteristics of this novel infectious disease. Though COVID-19 cases were reported from 198 countries or regions, and over 400,000 people were confirmed to be infected globally (24th March 2020)[8], it's transmission dynamics within the human population was unclear, so WHO designed a protocol for the countries to investigate the COVID-19 outbreaks locally and emphasized COVID-19 surveillance to understand the country situation[9].

Bangladesh, a country in Southeast Asia, exhibited different epidemiological features compared to other countries regarding the influenza virus in terms of seasonality, severity, and mortality[10,11]. On 8th March 2020, the first three cases of confirmed COVID-19 were reported in Bangladesh[12], and subsequently, the number of confirmed cases and deaths increased: at the end of the first month, there were 51 confirmed cases with five deaths from COVID-19[13]. As COVID-19 was a novel virus, there was minimal information regarding its severity and magnitude in Bangladesh.

The government of Bangladesh (GoB) initiated several efforts for the early detection of the virus to mitigate the spread: screening of passengers at airports, land ports, and maritime ports; hotline system to notify any suspected case of COVID-19 to the Institute of

Epidemiology, Disease Control and Research (IEDCR) so that their specimens could be collected and tested. Moreover, passengers arriving from countries with COVID-19 outbreaks were screened at the point of entries (PoE) and monitored for any symptom onset for 14 days, considering the virus's incubation period recommended by the WHO. However, these efforts were not enough to detect COVID-19 patients, as asymptomatic COVID-19 carriers already unfolded in their community and spread the virus in different geographical locations across Bangladesh. Patients with COVID-19 symptoms were reported from different hospitals and needed to be tested for diagnosis and treatment purposes. Thus, as a part of the pandemic preparedness and responses, there was an immediate need to establish a hospital-based platform to screen suspected COVID-19 patients to support GoB in hospitals where PCR-based COVID-19 testing facility was not available. The GoB initiated a countrywide system for detecting COVID-19 cases by prioritizing divisional hospitals, medical college hospitals, and few specialized hospitals to screen and test for COVID-19. Moreover, there was a knowledge gap on clinical and epidemiological data of COVID-19 patients in Bangladesh during the initial phase of the pandemic from any sentinel sites involving multiple public and private hospitals across the country.

To support the containment efforts for COVID-19, International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b) and Institute of Epidemiology, Disease Control and Research (IEDCR) under the Bangladesh Ministry of Health and Family Welfare jointly conducted this surveillance in selected hospitals where there was no nearby PCR based COVID-19 testing facility. Moreover, these hospitals were prioritized by GoB considering the existing influenza surveillance platform to better understand the clinical and epidemiological characteristics of COVID-19 patients from the geographical, social, and demographic context of Bangladesh.

# Methods

### *Setting*

The surveillance was conducted at the outpatient department (OPD) and inpatient department (IPD) of four selected hospitals where patients sought healthcare with suspected COVID-19 symptoms. Selected hospitals were three public and one private hospital situated in different geographical locations across Bangladesh **(Figure 1)**. These were three secondary level government hospitals (Sadar Hospital, Hobiganj, General Hospital, Potuakhali, District Hospital, Narshingdi) and one tertiary level private medical college hospital (Jahurul Islam Medical College hospital, Kishoregonj). To select these hospitals, we identified national Influenza surveillance/hospital-based Influenza surveillance sites, where there was no nearby polymerase chain reaction (PCR) test facility but a high load of potential suspected COVID-19 patients. It was considered that additional support to these hospitals would strengthen COVID-19 case identification and reporting at the national level.

### *Patient enrolment*

Within three months of the first COVID-19 case detection in the country, we deployed two trained staff in each selected hospital for screening suspected COVID-19 patients among all the patients attending the fever clinic at OPD and among all inpatients admitted into the specific wards (medicine ward, pediatric ward, intensive care unit (ICU) and COVID-19 isolation ward). They actively screened for suspected COVID-19 patients using a case definition applied by the GoB (patient with any one or more of the following symptoms within last 7 days- fever, cough, sore throat, and respiratory distress). Our surveillance staff at each hospital worked with hospital physicians to enroll suspected COVID-19 patients.

### *Data collection*

After obtaining written informed consent from those who met the suspected COVID-19 case definition, our staff collected data on socio-demographics, travel history, and clinical characteristics from them. Surveillance staff used proper personal protective equipment (PPE) during data and specimen collection. Field staff used tablet computers to collect data syncing with local icddr,b server using mobile internet. This system allowed real-time monitoring of the situation across all hospitals by the research team centrally from Dhaka city. After 30 days of enrollment, the surveillance team followed up with each enrolled patient through mobile phone calls to register the outcome of their illnesses and updated the database accordingly.

***Specimen collection***

Our field staff collected nasopharyngeal (NP) swabs from the enrolled patients. They collected the specimens into the virus transportation medium (VTM) and stored in a cool box at 2-4 degree °C temperature. Every evening, a porter transported all collected VTMs to icddr,b, Dhaka.

***Laboratory testing***

Nasopharyngeal swabs were tested for SARS-CoV-2 at the Virology Laboratory of icddr,b. RNA was extracted from nasopharyngeal swab using QiaAmp Viral RNA Mini kit (Qiagen, Hilden, Germany). RNA was tested for SARS-CoV-2 by real-time reverse transcription polymerase chain reaction (rRT-PCR) targeting SARS-CoV-2 specific ORF1ab- and N-gene. Any person with an rRT-PCR positive test result was defined as a laboratory-confirmed COVID-19 case/patient.

***Reporting to IEDCR, surveillance hospitals, and patients***

We received the laboratory test results on the following day of specimen collection. Our research team then shared the results with respective hospital authorities, district civil surgeons, divisional health directors, and the director of IEDCR over email. Moreover, we sent a text message (Short Message Service- SMS) to each enrolled patient informing their test report within 36 hours of specimen collection. Our investigators also responded to every query when any COVID-19 positive patient called them over the telephone upon getting the test result. The respective health care facilities then managed the patients following the existing government system.

***Data analysis***

The data management and analysis were performed using the software Stata v.13 (Stata Corp LP, College Station, TX, USA). We summarized all categorical variables using frequency and percentage. We also summarized using mean and standard deviation (SD) for symmetrically distributed variables and median and interquartile range (IQR) for asymmetrically distributed variables. We performed Pearson's $\chi^2$ test to compare the categorical variables and considered $p<0.05$ as statistically significant. We used univariate regression analysis for the interpretation of the outcome variable.

***Ethical consideration***

The protocol was reviewed and approved by the institutional review boards (IRB; Research Review Committee and Ethical Review Committee) of the International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b). We obtained written, informed consent of the participants before enrollment.

***Patient and public involvement***

It was not appropriate to involve patients or the public in the design, or conduct, or reporting, or dissemination plans of our study.

## Results

During 10th June to 31st August 2020, we enrolled 2,345 suspected COVID-19 patients from four selected hospitals; of them, 922 (39.3%) were laboratory-confirmed COVID-19 patients. The median age of the confirmed COVID-19 patients was 38 years (Interquartile range, IQR: 30-50 years), and 71% were male. COVID-19 was mostly detected among patients aged between 21-40 years (51.3%). About half of the COVID-19 positive patients (50.7%) had a higher level of education (>12 years). We identified 13% of the patients meeting surveillance case definition were healthcare workers (HCW), and they constituted 9% of all confirmed COVID-19 patients **(Table 1)**. Over the three months of the surveillance period, the peak of the COVID-19 positivity among suspected COVID-19 patients was detected in the 24$^{th}$ and 25$^{th}$ epi weeks (2$^{nd}$ and 3$^{rd}$ week of July 2020). The proportion of test positivity over time dropped and gradually started declining from the epi week 28$^{th}$ (2$^{nd}$ week of August) (**Figure 2 A**). We observed a relatively hard-to-reach riverside area (Patuakhali hospital) reporting the highest number and proportion of cases (355/793; 45%) compared to other hospitals in Narshingdi (313/796; 39%), Kishoreganj (144/462; 31%), and Habiganj (110/294; 37%), (**Figure 1 and Figure 2 B**). Most of the patients meeting the suspected COVID-19 case definition (91%) were identified from the outpatient departments of all the surveillance hospitals, and of them, 40% were COVID-19 positive. In contrast, among all patients enrolled from the inpatient departments, 28% were found COVID-19 positive.

The presenting clinical features in all suspected COVID-19 patients varied from dry cough (most common, 67%) to rash (least common, 0.4%), (**Figure 3A**). We found fever ≥ 38◦ C (53% vs. 44%), loss of taste (41% vs. 30%), headache (33% vs. 27%), fatigue (30% vs. 21%), loss of smell (23% vs. 13%), nausea/vomiting (18% vs. 15%) and joint pain (13% vs. 9%) were more likely to be the presenting clinical features among COVID-19 positive patients compared to the negative patients (all $p<0.05$). On the other hand, though sore throat was a very common feature among suspected COVID-19 patients, it was less common in the COVID-19 positive patients than COVID-19 negative patients (38% vs. 45%, $p=0.002$)

(**Figure 3A**). Besides, shortness of breath (47% vs. 22%) and vomiting (29% vs. 7%) were more common clinical characteristics of COVID-19 positive patients admitted in the hospitals compared to COVID-19 patients who attended at outpatients (**Figure 3B**). However, fever (54% vs. 40%), sore throat (41% vs. 9%), runny nose (24% vs. 7%), loss of smell (24% vs. 9%) and joint pain (14% vs. 2%) were more common clinical symptoms in COVID-19 patients at OPD compared to COVID-19 patients at IPD (All p values $<0.05$).

Compared to COVID-19 negative patients, patients with co-morbidities reported more infection with SARS-CoV-2, such as for chronic liver disease (51% vs. 39%), cardiovascular disease (43% vs. 39%), and diabetes (48% vs. 38%). Of these co-morbidities, diabetic patients showed significantly high susceptibility ($p < 0.05$) of getting infected than non-diabetic patients (**Figure 3C**). Other than these co-morbidities, we also found 19 cancer patients meeting enrolment criteria; of them, four patients (21%) were COVID-19 positive; and among positive, one (25%) died.

Among the 922 laboratory-confirmed COVID-19 patients, 21 (2.3%) patients were dead from our routine follow-up after a month of enrolment. Of them, 76% (16/21) patients died at the same enrolment hospital or different hospitals, 24% (5/21) patients died at home or on the way to the hospital. From the onset of symptoms, 43% (9/21) of patients died within 7 days, and 95% (20/21) deaths occurred within 15 days (**Supplementary Table 1**). When we compared epidemiological factors for association with adverse outcome of their clinical progression, our data showed that death was more likely to occur among patients presenting with age ≥ 60 years (OR:13.5; 95% CI: 5.4-33), shortness of breath (OR:14.4; 95% CI: 4.8-43), co-morbidity (OR:13.9; 95% CI: 3.2-60), smoking history (OR:3.9, 95% CI: 1.5-9.8), attending to a hospital in <2 days from the onset of symptoms due to critical illness (OR: 5.4; 95% CI: 1.8-17.1) and hospital admission (OR:13.3; 95% CI: 5.3-33.1; **Table 2**).

## Discussion

This sentinel surveillance identified 39% of patients as laboratory-confirmed COVID-19 among the suspected COVID-19 patients (patients with fever/cough/sore throat/respiratory distress) attending the surveillance hospitals from June to August 2020. Though our data showed more than one-third of the suspected patients were COVID-19 positive, this could be an underestimation; the true burden of this disease in terms of detection rate could be much higher considering the asymptomatic cases in the community and a smaller number of mild symptomatic cases seeking healthcare. Enrolling asymptomatic cases was beyond the scope of this surveillance; however many COVID-19 positive patients remain asymptomatic and possible sources of spreading infection at community[6,14,15]. Moreover, several socio-cultural factors and stigma, administrative malfunction, insecurity, misinformation, and poor trust in treatment- all have a negative impact on Bangladeshi people to seek healthcare and test for COVID-19[16]. Therefore, fewer people might seek healthcare from hospitals and undertake tests for this novel coronavirus through our surveillance platform, and hence, the real burden of COVID-19 could be even more.

COVID-19 suspected patients were found more at OPD than inpatient department, indicating that patients with COVID-19 symptoms were primarily mild, thereby seeking treatment from the OPD. Like any hospital-based survey, this surveillance only captured a portion of the symptomatic patients in the community who sought treatment from the surveillance hospitals. The percent positive ("percent positive rate" or "positivity rate") helps public health officials to assess the disease burden. COVID-19 positivity rate among the tested patients was increasing till July, followed by a gradual decline (**Figure 2A**). There was a sharp drop in specimen collection in the first week of August due to "Eid holidays" the biggest religious festival for Muslims. During this surveillance period, the percentage of COVID-19 positivity among tested samples was higher enough to draw public health attention. This is quite rational as this sentinel surveillance was strictly supervised and monitored by a team of dedicated researchers for the utmost quality of specimen and data collection from actual symptomatic patients and rapid transportation of specimens from remote field sites to central laboratory at Dhaka maintaining recommended standard temperature for rRT-PCR testing.

The national health system intended to collect specimens from symptomatic individuals, but there was no option/resource for such verification so that some asymptomatic individuals could be included. Moreover, people seeking a routine COVID-19 PCR test as a requirement for international travel was also included in the national system for COVID-19 reporting. In contrast, surveillance staff and physicians strictly verified the symptoms reported by each patient before enrolment and sample collection through the sentinel surveillance platform. Thereby, a robust sentinel COVID-19 surveillance is so important to better understand the actual disease situation in different administrative regions of a country. Continuing a sentinel surveillance system can explore the existing gap/weaknesses of COVID-19 and other disease burden estimation by closely and directly monitoring the situation in a particular area.

During the initial days of the COVID-19 crisis, there was a deficiency of adequate data to make appropriate policy decisions for Bangladesh[17]. Providing timely test reports and feeding peripheral sites' data from our surveillance hospitals to the government recording system greatly enhanced the management of the novel coronavirus crisis. Moreover, our work generated some key information about the ongoing COVID-19 pandemic in Bangladesh. More than half of our coronavirus positive patients were adults, 21-40 years old. This was consistent with the WHO report for Bangladesh (46.7%) (MMWU, 14 Sept 2020). Among COVID-19 positive patients, the male was predominant (71%), which might be due to the male-dominant societies' unique health-seeking behavior like Bangladesh, where women do not seek healthcare unless severe[18]. This finding was almost similar (68% male) during March-April, the early phase of novel coronavirus detection in Bangladesh[19]. Other than male predominance, more than half (51%) of the COVID-19 positive patients were found to be educated for 12 years or more. This might not be the cause that educated people were more infected than less educated or uneducated; rather it may be people with higher education were more conscious and thus were coming to hospitals for testing.

Chartterjee et. al reported that 5% of symptomatic HCWs were SARS-COV-2 positive in India[20]. Among COVID-19 suspected healthcare workers from our hospitals, one out of four was SARS-CoV-2 infected (27%). This was not a surprise because healthcare workers remain vulnerable to infectious disease in any low- and middle-income countries (LMICs) such as Bangladesh and demand adequate preparedness to fight against COVID-19[21]. Our findings also support that HCWs were getting infected at a much higher rate than India and, even more than that of a COVID-19 dedicated tertiary care hospital in Dhaka (11%)[22], Bangladesh. So, appropriate measures should be taken to prevent primary infection from patients and secondary infection from colleagues. Appropriate measures such as Infection Prevention and Control training, adequate PPE supply, and their proper use should be taken into consideration with high priority to protect HCWs from getting infected from their workplace.

Clinical features widely vary from asymptomatic infection (40% to 45% of SARS-CoV-2 infections) to death from acute respiratory distress syndrome (ARDS)[5,6,23]. Chinese researchers reported fever, cough, and expectoration were the commonest symptoms[24] in a multi-centered study. Another meta-analysis[25] revealed fever (88.7%), cough (57.6%), and dyspnea (45.6%) were the prominent presentation. We found cough followed by fever as the top two presenting symptoms of COVID-19 patients. It can be for our case definition too. Additionally, sore throat, loss of taste and loss of smell, headache, muscle& joint pain were more likely to occur among laboratory-confirmed COVID-19 patients. Nothing conclusive, but these differences could be used carefully by the treating physicians to manage a suspected COVID-19 patient initially before getting the lab report.

Comorbidities play a crucial role towards disease progression. Diabetes was the most commonly reported factor towards the adverse outcome of COVID-19 patients and their disease progression[26], requiring more hospitalization (18% vs. 8%) in the ICU and associated with more death compared to non-diabetic COVID patients[27]. Our surveillance data showed that diabetic patients were more susceptible to get a COVID-19 infection than others. So, besides other co-morbidities such as cardiovascular diseases, clinicians should consider additional clinical measures to manage a COVID-19 positive diabetic patient.

Mortality rate is one of the key indicators in public health. Our surveillance data revealed that the percentage of death among our COVID-19 positive patients was a little higher, 2.3%, than the global average death rate, 2.2% (2,737,370/124,363,841) as of 22nd March 2021. This death rate was possible to capture due to the unique post-discharge telephone follow up of enrolled patients after 30 days of enrollment for their outcome. Among all COVID-19 positive patients identified through the surveillance, we detected only 28% death (6/21) from the surveillance hospitals, the remaining 72% deaths (18/21) were possible to capture from this unique follow-up strategy of our sentinel surveillance system.

According to our findings, elderly, co-morbidity, having breathing difficulty, smoking, and admission in the inpatient department due to more severe illness were more likely to be the risk factors for death among the SARS-CoV-2 infected patients.

Regarding gender, Italy reported more death among men than women[28]. Nationally, Bangladesh has more COVID-19 deaths among men (76%) than women (24%)[29], but we did not find any significant difference in death rate between males and females from our surveillance. A nationwide analysis in China showed that age between 65 and 74 years, coronary heart disease, cerebrovascular disease, dyspnea were independent risk factors associated with fatal outcome[30]. China CDC analyzed 44,000 COVID patients' data and reported elderly, diabetes, cardiovascular disease, hypertension and chronic respiratory disease were all associated with an increased risk of death[31]. In the United Kingdom, people aged over 70 years with cardiovascular and respiratory diseases were considered as high-risk group[32]. Smoking was associated with increased risks of COVID-19 death and disease progression, a finding similar to other studies[33–36]. The WHO also mentioned increased severity of disease and mortality in hospitalized COVID-19 patients among smokers[37]. One meta-analysis reported a pooled OR of 1.89 (95% CI: 1.10-3.24) on the severity of this disease among smokers than non-smokers[35]. Another systematic review reported a significant association between smoking and the progression of COVID-19 (OR: 1.91; 95% CI: 1.42-2.59); the authors commented that the actual risk of smoking might be higher[38]. So, we recommend quit smoking to all, whether COVID-19 infected or not, for a better outcome during this pandemic. The surveillance data also showed more deaths occurred among critically ill hospitalized patients, which is natural. Thereby, an improved referral system from a district-level hospital to a tertiary level or specialized hospital could be considered for high-risk patients, which might reduce mortality.

Despite all efforts, our work had certain limitations. Based on our available resources and government priority, we conducted this surveillance at only four hospitals in different locations and enrolled suspected patients for three months only, with an additional one-month follow-up period. Thus, our findings might not be generalized for the whole Bangladeshi population. Moreover, we also missed the true prevalence of COVID-19 patients as we did not screen any asymptomatic patients. We only reported hospital-based prevalence because it was beyond the scope of this platform to estimate the community burden of COVID-19 in Bangladesh.

## Conclusion

Of the patients attending the surveillance hospitals with COVID-19 symptoms during the reporting period, more than one-third had a laboratory-confirmed COVID-19 and, this was more common among outpatients with peak positivity in July. Age ≥ 60 years, shortness of breath, co-morbid condition, smoking history, severe illness requiring hospital treatment were identified as the factors associated with death among COVID-19 patients. Though a small initiative, our COVID-19 sentinel surveillance revealed many key findings for the policymakers to understand this pandemic in the country context. Our effort strengthened government's capacity for rapid case detection, reporting, and quick containment efforts. Continuing this sentinel surveillance platform can better characterize disease patterns in populations over time, thus support the government by assessing the magnitude of the health problem and developing a data-driven effective management strategy as well as can monitor the progress towards the reduction of COVID-19 cases after corona vaccination campaign.

**Contributors:** The study concept was developed by FC and PD. The protocol was drafted by PD and critically revised by FC, SB, MR (Mahmudur Rahman), MR (Mahbubur Rahman), AA, TS, and MF. Data extraction and quality assessment was performed by ZA, SM AI and PD. Laboratory aspect was managed by ZR and MR (Mustafizur Rahman). PD developed the first draft manuscript. MR (Mahbubur Rahman), MB, SB, and all other authors provided feedback for all sections of the protocol including the design, analysis and revising the manuscript. All authors have approved the final version of the manuscript.

**Data availability statement:** Data cannot be made publicly available because these are confidential. Data are available from the respective department of icddr,b (www.icddrb.org) for researchers who meet the criteria for access to confidential data.

**Data sharing statement:** No additional data available.

**Disclaimer:** Our funding sources had no role in the design of the protocol, and was not involved during the methodological execution, data analyses and interpretation and decision to submit or to publish the study results.

**Patient and public involvement:** Due to the design of this study, it was not appropriate to involve patients and/or the public themselves in the design, or conduct, or reporting, or dissemination plans of this research.

**Ethics statements:** The protocol was reviewed and approved by the institutional review boards (IRB; Research Review Committee and Ethical Review Committee) of the International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b). We obtained written, informed consent of the participants before enrollment.

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**Conflicts of Interest:** The authors declare no conflict of interest.

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**Table 1.** Socio-demographic characteristics of suspected COVID-19 patients in selected hospitals of Bangladesh, June-August 2020

| Characteristics | | Suspected COVID-19 patients (N=2345) | SARS-CoV-2 Positive by rRT-PCR | | |
|---|---|---|---|---|---|
| | | | Total Positive (922) | Inpatient (57) n (%) | Out-patient (865) n (%) |
| Age (in years) | | | | | |
| | Median (IQR) | 35 (26-48) | 38 (30-50) | 55 (45-69) | 38 (29-48) |
| Age sub-groups | | | | | |
| | 0-5 | 25 (1.11) | 6 (0.7) | 1 (1.7) | 5 (0.6) |
| | 6-10 | 30 (1.3) | 11 (1.2) | 0 (0) | 11 (1.3) |
| | 11-20 | 167 (7.1) | 42 (4.5) | 0 (0) | 42 (4.8) |
| | 21-30 | 684 (29.1) | 228 (24.7) | 5 (8.7) | 223 (25.8) |
| | 31-40 | 594 (25.3) | 246 (26.6) | 6 (10.5) | 240 (27.7) |
| | 41-50 | 382 (16.3) | 182 (19.7) | 11 (19.3) | 171 (19.7) |
| | 51-60 | 267 (11.4) | 125 (13.5) | 8 (14.0) | 117 (13.5) |
| | 60+ | 196 (8.3) | 82 (8.8) | 26 (45.6) | 56 (6.5) |
| Sex | | | | | |
| | Male | 1590 (67.8) | 654 (70.9) | 38 (66.7) | 616 (71.2) |
| Occupation | | | | | |
| | HCW | 302 (12.9) | 83 (9.0) | 2 (3.5) | 81 (9.4) |
| | Service | 946 (40.3) | 431 (46.8) | 7 (12.3) | 424 (49.0) |
| | Business | 154 (6.6) | 82 (8.9) | 6 (10.5) | 76 (8.8) |
| | Student | 223 (9.5) | 68 (7.4) | 0 (0) | 68 (7.9) |
| | Dependent | 215 (9.1) | 73 (7.9) | 22 (38.6) | 51 (5.9) |
| | Unemployed | 145 (6.1) | 64 (6.9) | 9 (15.8) | 55 (6.3) |
| | Others* | 360 (15.3) | 121 (13.1) | 11 (19.3) | 110 (12.7) |
| Education (years) | | | | | |
| | No formal schooling | 155 (6.6) | 44 (4.8) | 11 (19.3) | 33 (3.8) |
| | 1-5 | 255 (10.9) | 89 (9.7) | 11 (19.3) | 78 (9.0) |
| | 6-10 | 496 (21.2) | 178 (19.3) | 22 (38.6) | 156 (18.0) |
| | 11-12 | 367 (15.7) | 144 (15.6) | 7 (12.3) | 137 (15.8) |
| | >12 | 1072 (45.6) | 467 (50.7) | 6 (10.5) | 461 (53.4) |

**Farmer, day-labour, small shop owner, rickshaw/van puller, driver etc.*

**Table 2.** Factors associated with adverse outcome (death) among COVID-19 positive patients in selected hospitals of Bangladesh, June-August 2020.

| **Factors** | | **Frequency N=922** | **Death n=21** Frequency (%) | **Odds ratio (OR)** | **95% CI** |
|---|---|---|---|---|---|
| Age* | 0-59 years | 812 | 8 (1%) | 1 | |
| | ≥ 60 years | 110 | 13 (11.8%) | 13.5 | 5.4-33.3 |
| Sex | Male | 654 | 14 (2.1%) | 1 | |
| | Female | 268 | 7 (2.6%) | 1.2 | 0.5-3.0 |
| Health care worker | Yes | 83 | 0 (0%) | 1 | |
| | No | 839 | 21 (2.5%) | 1.0 | - |
| Symptoms | ≤3 symptoms | 314 | 7 (2.2%) | 1 | |
| | >3 symptoms | 608 | 14 (2.3%) | 1.0 | 0.4-2.5 |
| Shortness of breath* | No | 700 | 4 (0.6%) | 1 | |
| | Yes | 222 | 17 (7.7%) | 14.4 | 4.8-43 |
| Comorbidity* | No | 538 | 2 (0.4%) | 1 | |
| | Yes | 384 | 19 (4.9%) | 13.9 | 3.2-60 |
| History of smoking* | No | 812 | 14 (1.7%) | 1 | |
| | Yes | 110 | 7 (6.4%) | 3.9 | 1.5-9.8 |
| Treatment received from* | OPD | 865 | 12 (1.4%) | 1 | |
| | inpatient | 57 | 9 (15.8%) | 13.3 | 5.3-33.1 |
| Duration of hospital attendance from the onset of symptom* | ≥ 2 days | 880 | 17 (1.9%) | 1 | |
| | < 2 days | 42 | 4 (9.8%) | 5.4 | 1.8-17.1 |

***Factors with a significant difference between groups***

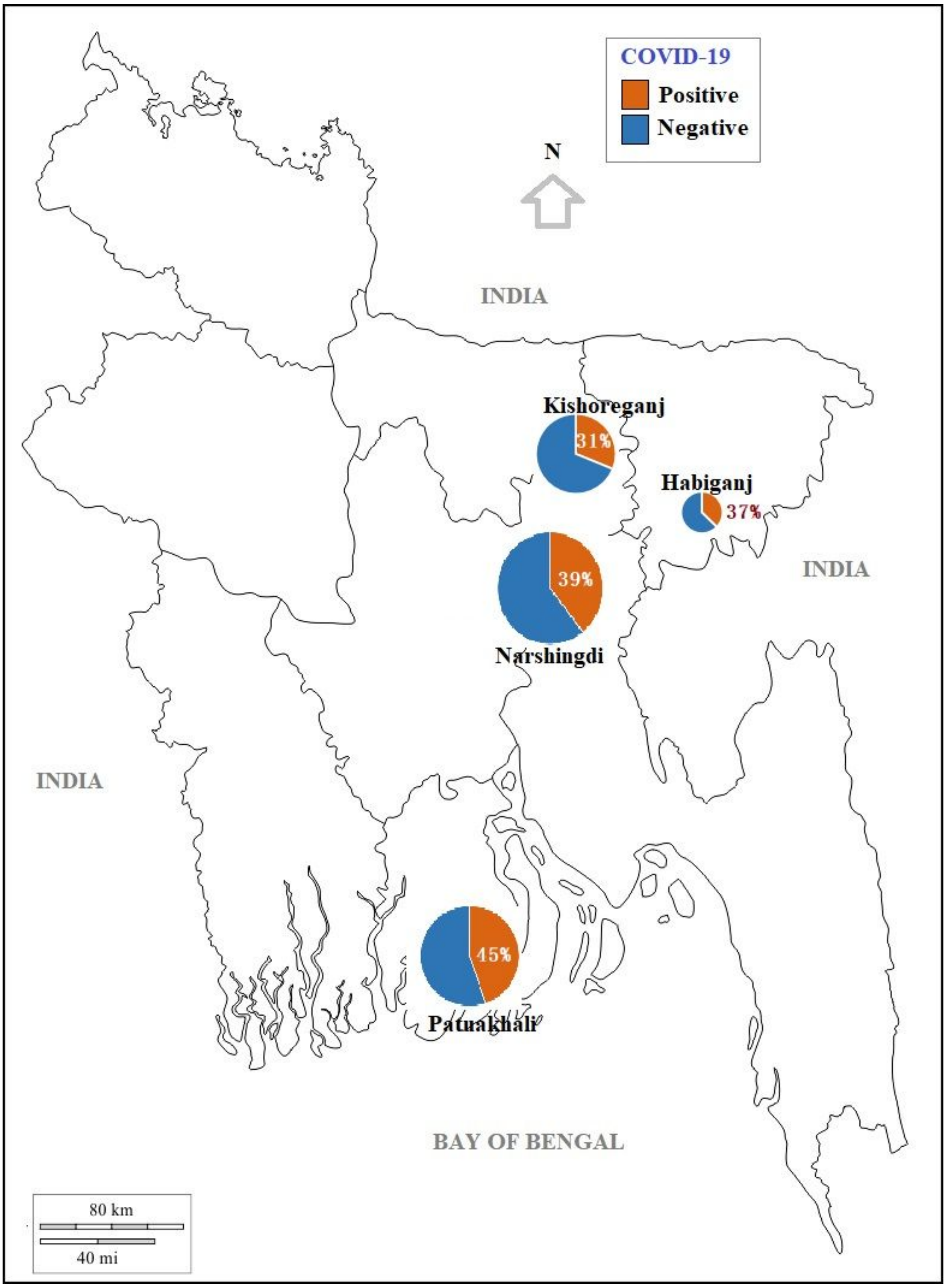


**Figure 1.** Location of the study hospitals and proportionate distribution of enrolled patients at different sites with their COVID-19 positivity, June to August 2020

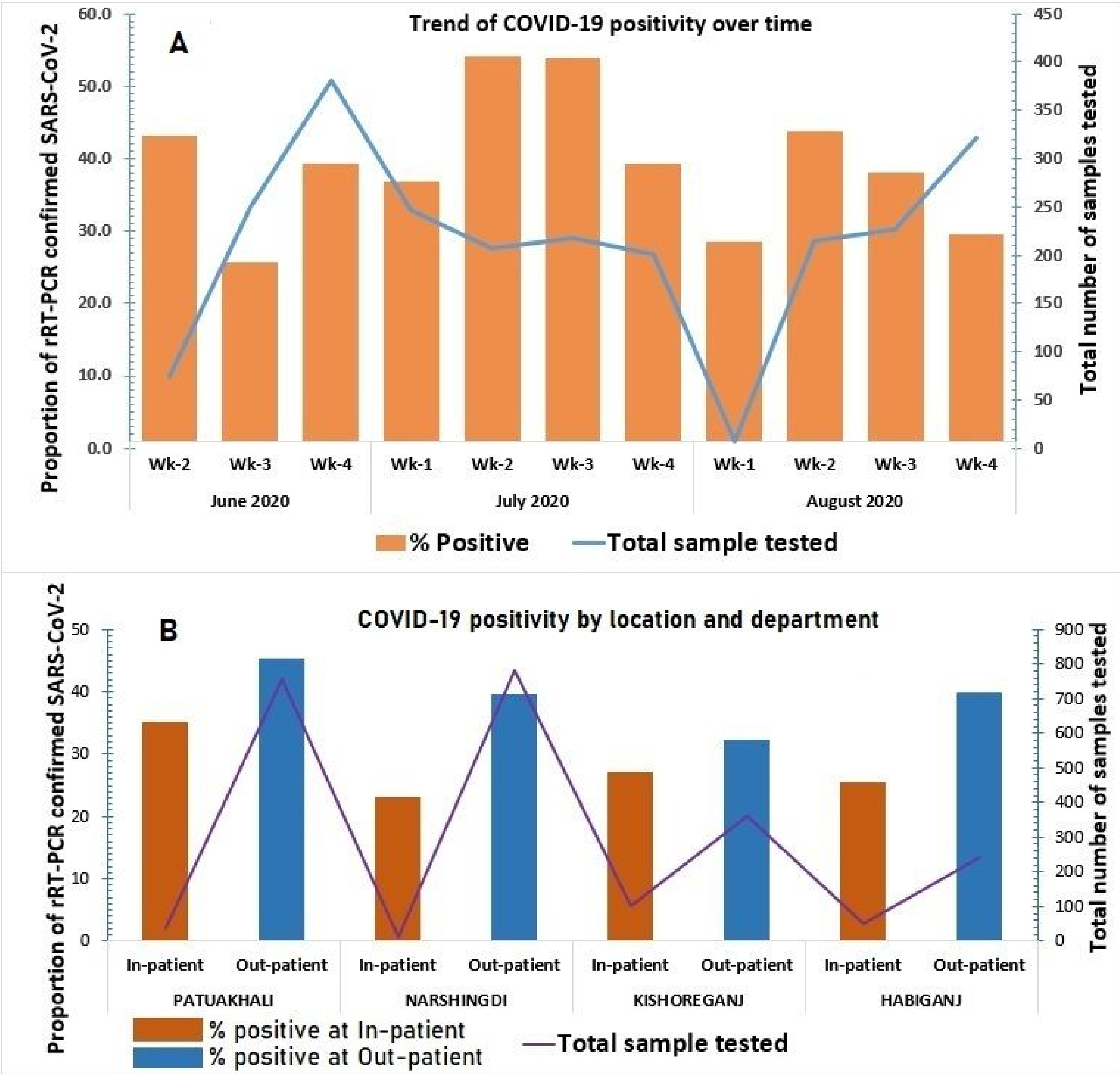


**Figure 2.** SARS-CoV-2 infection among suspected COVID-19 patients at inpatient and outpatient departments of selected hospitals during June to August 2020, Bangladesh

A- Detection of SARS-CoV-2 at all four selected hospitals over time
B- Detection of SARS-CoV-2 at inpatient and outpatient departments of selected hospital sites

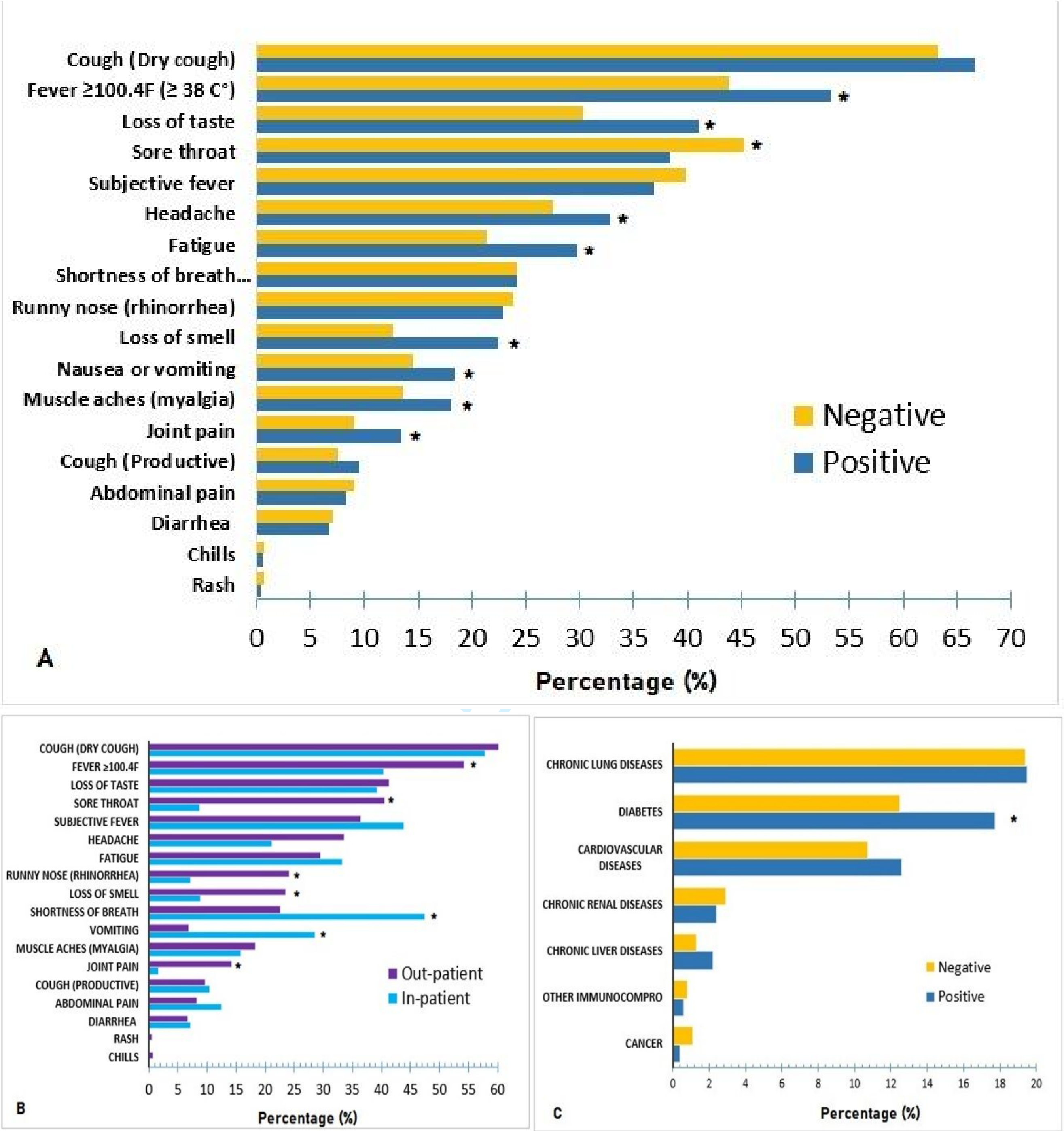


**Figure 3. Distribution of SARS-CoV-2 infected patients by their clinical features and comorbidity in selected hospitals of Bangladesh, June-August 2020**

A. Presenting symptoms of all COVID-19 suspected patients by rRT-PCR results
B. Presenting symptoms of COVID-19 patients by department
C. COVID-19 positive patients by their comorbidity

**Supplementary table 1**. Distribution of deaths among COVID-19 positive patients in selected hospitals of Bangladesh, June-August 2020.

| | Hospital death n= 16 | | Home death n=5 | |
|---|---|---|---|---|
| **Age (years)** | | | | |
| Lowest, highest | 40, 85 | | 51, 90 | |
| Median (IQR) | 65 (55-69) | | 64 (52-70) | |
| **Sex** | | | | |
| Male | 11 (69) | | 3 (60) | |
| **Timing of death from symptom onset** | | | | |
| 0-7 days | 6 (38) | 6 (38) Cum. | 3 (60) | 3 (60) Cum. |
| 8-15 days | 9 (56) | 15 (94) | 2 (40) | 5 (100) |
| 16-40 days | 1 (6) | 16 (100) | | |
| **Manner of death** | | | | |
| Disease | 16 | | 5 (100) | |
| Accident | 0 | | 0 | |
| Sudden death (heart attack) | 0 | | 0 | |
| **Comorbidity present (anyone)** | 15 (94%) | | 4 (80) | |
| DM | 9 (56) | | 2 (40) | |
| Asthma/COPD | 4 (25) | | 2 (40) | |
| Heart disease/HTN | 6 (37) | | 2 (40) | |
| Chronic renal disease | 4 (25) | | 0 | |
| Cancer (uterine) | 1 (6) | | 0 | |
| **Clinical course of treatment** | | | | |
| Oxygen required | 16 (100) | | 3 (60) [ 2 got oxygen at home] | |
| ICU admitted | 3 (19) | | | |
| CCU admitted | 1 (6) | | | |
| Dialysis required | 1 (6) | | | |
| **Cause of death as stated from hospital as reported** | | | | |
| COVID-19 + Respiratory failure | 14 (88) | | | |
| Pneumonia | 1 (6) | | | |
| Chronic renal failure | 1 (6) | | | |

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

| | Item No | Recommendation | Page No |
|---|---|---|---|
| **Title and abstract** | 1 | (*a*) Indicate the study's design with a commonly used term in the title or the abstract | 1 |
| | | (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found | 1 |
| **Introduction** | | | |
| Background/rationale | 2 | Explain the scientific background and rationale for the investigation being reported | 4-5 |
| Objectives | 3 | State specific objectives, including any prespecified hypotheses | 5 |
| **Methods** | | | |
| Study design | 4 | Present key elements of study design early in the paper | 6 |
| Setting | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | 6-7 |
| Participants | 6 | (*a*) Give the eligibility criteria, and the sources and methods of selection of participants | 6 |
| Variables | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable | 8 |
| Data sources/ measurement | 8* | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group | *NA* |
| Bias | 9 | Describe any efforts to address potential sources of bias | NA |
| Study size | 10 | Explain how the study size was arrived at | NA |
| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why | 7 |
| Statistical methods | 12 | (*a*) Describe all statistical methods, including those used to control for confounding | 7 |
| | | (*b*) Describe any methods used to examine subgroups and interactions | 7 |
| | | (*c*) Explain how missing data were addressed | NA |
| | | (*d*) If applicable, describe analytical methods taking account of sampling strategy | |
| | | (*e*) Describe any sensitivity analyses | |
| **Results** | | | |
| Participants | 13* | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed | 8 |
| | | (b) Give reasons for non-participation at each stage | NA |
| | | (c) Consider use of a flow diagram | NA |
| Descriptive data | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders | 8-9 |
| | | (b) Indicate number of participants with missing data for each variable of interest | NA |
| Outcome data | 15* | Report numbers of outcome events or summary measures | 7-10 |
| Main results | 16 | (*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included | 10 |

| | | | |
|---|---|---|---|
| | | (*b*) Report category boundaries when continuous variables were categorized | NA |
| | | (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period | |
| Other analyses | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses | NA |
| **Discussion** | | | |
| Key results | 18 | Summarise key results with reference to study objectives | 10-15 |
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias | 15 |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence | 16 |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results | 15 |
| **Other information** | | | |
| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based | 16 |

*Give information separately for exposed and unexposed groups.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

# Establishing a sentinel surveillance system for the novel coronavirus disease 2019 (COVID-19) in a resource limited county: methods, system attributes and early findings

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| Secondary Subject Heading: | Epidemiology, Global health, Infectious diseases |
| Keywords: | COVID-19, Epidemiology < TROPICAL MEDICINE, Public health < INFECTIOUS DISEASES, Diagnostic microbiology < INFECTIOUS DISEASES, EPIDEMIOLOGY |
| | |

# Establishing a sentinel surveillance system for the novel coronavirus disease 2019 (COVID-19) in a resource limited county: methods, system attributes and early findings

Pritimoy Das[1,†], Zubair Akhtar[1], Syeda Mah-E-Muneer[1], Md Ariful Islam[1], Mohammed Ziaur Rahman[1], Mustafizur Rahman[1], Mahmudur Rahman[1], Mahbubur Rahman[2], Mallick Masum Billah[2], ASM Alamgir[2], Meerjady Sabrina Flora[2], Tahmina Shirin[2], Sayera Banu[1], Fahmida Chowdhury[1]

[1]Infectious Diseases Division, International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b), Dhaka, Bangladesh
[2]Institute of Epidemiology, Disease Control and Research (IEDCR), Dhaka, Bangladesh

[†]Correspondence to Pritimoy Das; pritimoydas@gmail.com



## ABSTRACT

**Objectives** To establish a hospital-based platform to explore the epidemiological and clinical characteristics of patients screened for COVID-19.

**Design** Hospital-based surveillance.

**Setting** This study was conducted in four selected hospitals in Bangladesh during 10th June to 31st August 2020.

**Participants** In total, two thousand three hundred and forty-five patients of all age (68% male) attending the outpatient and inpatient departments of surveillance hospitals with any one or more of the following symptoms within last 7 days- fever, cough, sore throat, and respiratory distress.

**Outcome measures** The outcome measures were COVID-19 positivity and mortality rate among enrolled patients. Pearson's $\chi^2$ test was used to compare the categorical variables (sign-symptoms, co-morbidities, admission status and COVID-19 test results). Regression analysis was performed to determine the association between potential risk factors and death.

**Results** COVID-19 was detected among 922 (39%) enrolled patients. It was more common in outpatients with a peak positivity in 2nd week of July (112, 54%). The median age of the confirmed COVID-19 cases was 38 years (IQR: 30-50), 654 (71%) were male, and 83 (9%) were healthcare workers. Cough (615, 67%) was the most common symptom, followed by fever (493, 53%). Diabetic patients were more likely to get COVID-19 than non-diabetic (48% vs. 38%; OR:1.5; 95% CI:1.2-1.9). The death rate among COVID-19 positive was 2.3%, n=21. Death was associated with age ≥ 60 years (AOR:13.9; 95% CI:5.5-34), shortness of breath (AOR:9.7; 95% CI: 3.0-30), co-morbidity (AOR:4.8; 95% CI:1.1-21.7), smoking history (AOR: 2.2, 95% CI:0.7-7.1), attending the hospital in <2 days of symptom onset due to critical illness (AOR: 4.7; 95% CI:1.2-17.8) and hospital admission (AOR:3.4; 95% CI: 1.2-9.8).

**Conclusions** COVID-19 positivity was observed in more than one-third of suspected COVID-19 patients attending selected hospitals. While managing such patients, the risk factors identified for higher death rates should be considered.

**Key words:** Bangladesh, COVID-19, hospital-based study, SARS-CoV-2, sentinel surveillance.

## Strengths and limitations of this study

- In collaboration with a government public health institution and an international research organization, we implemented a sentinel surveillance for COVID-19 in resource-constrained settings.
- This is a multicentre study with representative hospitals included from almost all major administrative regions of Bangladesh.
- Our surveillance method was unique in that we shared test results with patients and used a 30-day follow-up plan to track the prognosis of COVID-19 positive patients even after they were discharged from the enrolling hospital. As we did not test any asymptomatic patients and community burden estimation was beyond our scope, the true prevalence of COVID-19 patients might be higher than reported in our study.

## Introduction

Starting from its inception at Wuhan, Hubei Province, China, the novel coronavirus named severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has spread across the world within a few months, causing Coronavirus Disease 2019 (COVID-19).[1] Globally, 129,651,305 cases and 2.8 million deaths were recorded till 31th March 2021.[2] This virus manifests various clinical characteristics, from asymptomatic infection to severe pneumonia, vasculitis, and death.[3–6] It was declared a public health emergency of international concern (PHEIC) by the world health organization (WHO) in 30th January 2020 and subsequently a pandemic on 11th March 2020.[7] During that early stage of this coronavirus disease, there was uncertainty and variation regarding the epidemiological, clinical, and virological characteristics of this novel infectious disease. Though COVID-19 cases were reported from 198 countries or regions, and over 400,000 people were confirmed to be infected globally (24th March 2020),[8] its transmission dynamics within the human population was unclear, so WHO designed a protocol for the countries to investigate the COVID-19 outbreaks locally and emphasized COVID-19 surveillance to understand the country situation.[9]

Bangladesh, a country in Southeast Asia, exhibited different epidemiological features compared to other countries regarding the influenza virus in terms of seasonality, severity, and mortality.[10,11] On 8th March 2020, the first three cases of confirmed COVID-19 were reported in Bangladesh,[12] and subsequently, the number of confirmed cases and deaths increased: at the end of the first month, there were 51 confirmed cases with five deaths from COVID-19.[13] As COVID-19 was a novel virus, there was minimal information regarding its severity and magnitude in Bangladesh.

The government of Bangladesh (GoB) initiated several efforts for the early detection of the virus to mitigate the spread such as screening of passengers at airports, land ports, and maritime ports; hotline system to notify any suspected case of COVID-19 to the Institute of

Epidemiology, Disease Control and Research (IEDCR) so that their specimens could be collected and tested. Moreover, passengers arriving from countries with COVID-19 outbreaks were screened at the point of entries (PoE) and monitored for any symptom onset for 14 days, considering the virus's incubation period recommended by the WHO.[14] However, these efforts were not enough to detect COVID-19 patients, as asymptomatic COVID-19 carriers already unfolded in their community and spread the virus in different geographical locations across Bangladesh.[15] Patients with COVID-19 symptoms were reported from different hospitals and needed to be tested for diagnosis and appropriate treatment purposes.[16] Initially, there were 10 laboratories in capital Dhaka city and five laboratories outside Dhaka had COVID-19 testing facility in Bangladesh.[17] Thus, as a part of the pandemic preparedness and responses, there was an immediate need to establish a hospital-based platform to screen suspected COVID-19 patients to support GoB in hospitals where PCR-based COVID-19 testing facility was not available. The GoB initiated a countrywide system for detecting COVID-19 cases by prioritizing divisional hospitals, medical college hospitals, and few specialized hospitals to screen and test for COVID-19. Moreover, there was a knowledge gap on clinical and epidemiological data of COVID-19 patients in Bangladesh during the first wave of the pandemic from any sentinel sites involving multiple public and private hospitals across the country.

The quality of surveillance data in many developing countries is hampered by a variety of factors, including a lack of resources and training.[18] Ibrahim et al. (2020) looked into various COVID-19 surveillance activities around the world and categorized them into a systematic review paper of thirty articles.[19] Our surveillance falls into a combination of sentinel surveillance and enhanced surveillance of hospitalized cases in which risk groups can be identified, tested, and followed up on via a hospital and laboratory network. Current surveillance included searching for suspected COVID-19 patients among hospitalized patients as well as screening and testing patients from outpatient. In Singapore, a similar approach was taken for the investigation and confinement efforts for COVID-19.[20,21]

To support the containment efforts for COVID-19, the International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b) and the Institute of Epidemiology, Disease Control and Research (IEDCR) under the Bangladesh Ministry of Health and Family Welfare jointly conducted this surveillance in selected hospitals where there was no nearby PCR based COVID-19 testing facility. The aim of this study was to establish a hospital-based platform to describe and analyze epidemiological and clinical characteristics of patients screened for COVID-19 in selected Bangladeshi hospitals with limited resources during the first wave of COVID-19 pandemic of the pandemic.

## Methods

### *Setting*

The surveillance was conducted at the outpatient department (OPD) and inpatient department (IPD) of four selected hospitals where patients sought healthcare with suspected COVID-19 symptoms. There were three public hospitals and one private hospital, all of which were in different geographical locations across Bangladesh **(Figure 1)**. The public hospitals namely Sadar Hospital, Hobiganj (24°22'24.77", 91°25'3.62"), General Hospital, Potuakhali (22°21'52.19", 90°19'37.25" and District Hospital, Narshingdi (23°55' 48.6", 90°42' 9.84"), all having 100-250 number of beds. Jahurul Islam Medical College hospital, Kishoregonj (24°12' 2.26", 90°55'1.81") is a general tertiary level 500 bed teaching hospital. To select these hospitals, we evaluated the ongoing national hospital-based Influenza surveillance platforms to identify the hospitals where there was no in-hospital or nearby polymerase chain reaction (PCR) based COVID-19 testing facility at that time but a high load of potential suspected COVID-19 patients in that geographical location. It was considered that additional support to these hospitals would strengthen COVID-19 case identification and reporting at the national level with generation of epidemiological data.

***Patient enrolment***

Within three months of the first COVID-19 case detection in the country, we deployed two trained field staff in each selected hospital (total eight field staff placed in four hospitals) for screening suspected COVID-19 patients among all the patients attending the fever clinic at OPD and among all inpatients admitted into the specific wards (medicine ward, pediatric ward, intensive care unit (ICU) and COVID-19 isolation ward). These field staffs worked with hospital physicians to enroll suspected COVID-19 patients.

Case-definition: Field staff actively screened for suspected COVID-19 patients using the following case definition: patient with any one or more of the following symptoms within last 7 days- fever, cough, sore throat, and respiratory distress. This case definition was applied by GoB to collect samples as suspected COVID-19 patient.

***Data collection***

After obtaining written informed consent from patients who met the suspected COVID-19 case definition, field staff collected data on socio-demographics (age, sex, occupation, educational level), travel history (local or international travel), and clinical characteristics (presenting symptoms, clinical signs, comorbidity, admission status, smoking history, duration of symptom onset to treatment seeking) from them. Field staff used proper personal protective equipment (PPE) such as N95 mask/medical mask, disposable gown, disposable cap, disposable gloves, face shield and goggles during data and specimen collection. Field staff used tablet computers to collect data syncing with local icddr,b server using mobile internet. This system allowed real-time monitoring of the situation across all hospitals by the research team centrally from Dhaka city. After 30 days of enrollment, the surveillance team (field staff, their supervisor and occasionally, the first author) followed up with each enrolled patient through mobile phone calls to register the outcome of their illnesses and updated the database accordingly. The outcome variables were COVID-19 positivity by RT-PCR test and the mortality among the SARS-CoV-2 infected patients.

***Specimen collection and Transportation***

Trained field staff collected a single nasopharyngeal swab through swab stick from each enrolled patients in viral transportation medium (VTM) and stored in a cool box between 2-4 °C temperature. Inhouse (icddr,b lab) VTM preparation was used for the collected samples. Every afternoon, a dedicated porter transported all the samples to icddr,b, Dhaka using a private car from three surveillance hospitals except Patuakhali. From Patuakhali, one of the dedicated porter brought samples to icddr,b by launch (public transport). All VTMs were handed over to icddr,b virology laboratory within 24 hours of specimen collection.

***Laboratory testing***

Nasopharyngeal swabs were tested for SARS-CoV-2 at the Virology Laboratory of icddr,b. Ribonucleic acid (RNA) was extracted from nasopharyngeal swab using QiaAmp Viral RNA Mini kit (Qiagen, Hilden, Germany). RNA was tested for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by real-time reverse transcription polymerase chain reaction (rRT-PCR) targeting SARS-CoV-2 specific ORF1ab- and N-gene. Any person with an rRT-PCR positive test result was defined as a laboratory-confirmed COVID-19 case/patient.

***Reporting to IEDCR, surveillance hospitals, and patients***

We received the laboratory test results on the following day of specimen collection. Our research team then shared the results with respective hospital authorities, district civil surgeons, divisional health directors, and the director of IEDCR over email. Moreover, we sent a text message (Short Message Service- SMS) to each enrolled patient informing their test report within 36 hours of specimen collection. Our investigators also responded to every query when any COVID-19 positive patient called them over the telephone upon getting the test result. The respective health care facilities then managed the patients following the existing government system.

***Data analysis***

The data management and analysis were performed using the software Stata v.13 (Stata Corp LP, College Station, TX, USA). We summarized all categorical variables using frequency and percentage. We also summarized using mean and standard deviation (SD) for symmetrically distributed variables and median and interquartile range (IQR) for asymmetrically distributed variables. We performed Pearson's $\chi^2$ test to compare the categorical variables and considered $p<0.05$ as statistically significant. We used univariate logistic regression analysis for strengths of associations and identified risk factors for death, using odds ratio and adjusted for age and sex in the multivariable model.

***Ethical consideration***

The protocol was reviewed and approved by the institutional review boards (IRB; Research Review Committee and Ethical Review Committee) of the International Centre for Diarrhoeal Disease Research, Bangladesh (Ref. number PR-20032). We obtained written, informed consent of the participants before enrollment. To ensure anonymity of the study participants and maintain the confidentiality, the names and identifying information of the participants was and will not be shared with anyone outside of the data collection team and this information was kept in locked cabinets and/or computers with passwords. Laboratory specimens were identified only by patient enrolment ID. Necessary permission was obtained from the respective hospitals before establishing the hospital-based platform and data collection.

***Patient and public involvement***

Patients or the public were not involved in the study design, or conduct, or reporting, or dissemination plans.

## Results

*COVID-19 positivity and Demographic characteristics*

During 10th June to 31st August 2020, we enrolled 2,345 suspected COVID-19 patients from four selected hospitals. Virology Laboratory of icddr,b tested all the 2,345 nasopharyngeal swab samples collected from these enrolled participants; of them, 922 (39.3%) were laboratory-confirmed COVID-19 patients. The median age of the confirmed COVID-19 patients was 38 years (Interquartile range, IQR: 30-50 years), and 654 (71%) were male. COVID-19 was mostly detected among patients aged between 21-40 years (474, 51.3%). About half of the COVID-19 positive patients (467, 50.7%) had a higher level of education (>12 years). We identified 302 (13%) of the patients meeting surveillance case definition were healthcare workers (HCW), and they constituted 83 (9%) of all confirmed COVID-19 patients **(Table 1)**.

*Seasonality and geographical variation*

Over the three months of the surveillance period, the peak of the COVID-19 positivity among suspected COVID-19 patients was detected in the 24th and 25th epi weeks (2nd and 3rd week of July 2020). We observed a relatively hard-to-reach riverside area (Patuakhali hospital) reporting the highest number and proportion of cases (355/793; 45%) compared to other hospitals in Narshingdi (313/796; 39%), Kishoreganj (144/462; 31%), and Habiganj (110/294; 37%). The proportion of test positivity over time dropped and gradually started declining from the epi week 28th (2nd week of August) (**Figure 1 and Figure 2 A, B**).

*IPD vs. OPD visits*

Most of the patients meeting the suspected COVID-19 case definition (2141, 91%) were identified from the outpatient departments of all the surveillance hospitals, and of them, 865 (40%) were COVID-19 positive. In contrast, among all patients enrolled from the inpatient departments, 57 (28%) were found COVID-19 positive. Shortness of breath (97, 47% vs. 482, 22%) and vomiting (58, 29% vs. 146, 7%) were more common clinical characteristics of COVID-19 positive patients admitted in the hospitals compared to COVID-19 patients who attended at outpatients (**Figure 3B**). However, fever (1163, 54% vs. 82, 40%), sore throat (869, 41% vs. 18, 9%), runny nose (518, 24% vs. 14, 7%), loss of smell (503, 24% vs. 18, 9%) and joint pain (304, 14% vs. 3, 2%) were more common clinical symptoms in COVID-19 patients at OPD compared to COVID-19 patients at IPD (All p values $<0.05$).

*Differences in clinical presentation between COVID-19 positive and COVID-19 negative patients*

The presenting clinical features in all suspected COVID-19 patients varied from dry cough (most common, 67%, n=1562) to rash (least common, 0.4%, n=9), (**Figure 3A**). We found fever ≥ 38◦ C (1252, 53% vs. 1077, 44%), loss of taste (964, 41% vs. 711, 30%), headache (772, 33% vs. 645, 27%), fatigue (696, 30% vs. 499, 21%), loss of smell (528, 23% vs. 295, 13%), nausea/vomiting (431, 18% vs. 340, 15%) and joint pain (314, 13% vs. 223, 9%) were more likely to be the presenting clinical features among COVID-19 positive patients compared to the negative patients (all $p<0.05$). On the other hand, though sore throat was a very common feature among suspected COVID-19 patients, it was less common in the COVID-19 positive patients than COVID-19 negative patients (900, 38% vs. 1060, 45%, $p=0.002$) (**Figure 3A**).

*Comorbidities among COVID-19 patients*

Compared to COVID-19 negative patients, patients with co-morbidities reported more infection with SARS-CoV-2, such as for chronic liver disease (20, 51% vs. 898, 39%), cardiovascular disease (116, 43% vs. 801, 39%), and diabetes (164, 48% vs. 755, 38%). Of these co-morbidities, diabetic patients showed significantly high susceptibility ($p < 0.05$) of getting infected with SARS-CoV-2 than non-diabetic patients (**Figure 3C**). Other than these co-morbidities, we also found 19 cancer patients meeting enrolment criteria; of them, four patients (21%) were COVID-19 positive; and among positive, one (25%) died.

*Mortality and associated risk factors*

Among the 922 laboratory-confirmed COVID-19 patients, 21 (2.3%) patients were reported dead from our routine follow-up after a month of enrolment. Of them, 76% (16/21) patients died at the same enrolment hospital or different hospitals, 24% (5/21) patients died at home or on the way to the hospital. From the onset of symptoms, 43% (9/21) of patients died within 7 days, and 95% (20/21) deaths occurred within 15 days (**Supplementary Table 1**). When we compared epidemiological factors for association with adverse outcome of their clinical progression, our data showed that death was more likely to occur among patients presenting with age ≥ 60 years (AOR:13.9; 95% CI: 5.5-34.5), shortness of breath (AOR:9.7; 95% CI: 3.0-30), co-morbidity (AOR:4.8; 95% CI: 1.1-21.7), smoking history (AOR:2.2, 95% CI: 0.7-7.1), attending to a hospital in <2 days from the onset of symptoms due to critical illness (AOR: 4.7; 95% CI: 1.2-17.8) and hospital admission (AOR:3.4; 95% CI: 1.2-9.8; **Table 2**).

## Discussion

Our hospital-based COVID-19 sentinel surveillance platform identified more than one-third (39%) of patients as laboratory-confirmed COVID-19 among the suspected COVID-19 patients attending the hospitals during the study period. This COVID-19 positivity rate was much higher to draw public health attention compared to WHO reported national data (19.5%) from 8th March to 14th September 2020.[22] The national health system intended to collect specimens from symptomatic individuals, but considering resource constrain verification of symptoms was difficult and thereby some asymptomatic individuals could be included for testing. Moreover, people seeking a routine COVID-19 PCR test as a requirement for international travel was also included in the national system for COVID-19 reporting. In contrast, surveillance staff and physicians strictly verified the symptoms reported by each patient before enrolment and sample collection through the sentinel surveillance platform. This sentinel surveillance was strictly supervised and monitored by a team of dedicated researchers for the utmost quality of specimen and data collection from actual symptomatic patients and rapid transportation of specimens from remote field sites to central laboratory at Dhaka maintaining recommended standard temperature for rRT-PCR testing. Thereby, a robust sentinel COVID-19 surveillance is so important to better understand the actual disease burden in different administrative regions of a country.

More than half of our COVID-19 positive patients were young adults within the age group of 21-40 years. This was consistent (46.7%) with the WHO report for Bangladesh on morbidity and mortality weekly update (MMWU) as of 14th Sept 2020.[22] Among the COVID-19 positive patients, male was predominant. This was consistent with other nearby countries such as India, where researcher reported that male COVID-19 cases (65.39%) were more than females (34.61%).[23] This might be due to the male-dominant societies' unique health-seeking behavior like Bangladesh, where women do not seek healthcare unless severe.[24] This finding was similar (68% male) during March-April, the early phase of novel coronavirus detection in Bangladesh.[25] Other than male predominance, more than half of the COVID-19 positive patients were found to be educated for 12 years or more. This might not be the cause that educated people were more infected than less educated or uneducated; rather it may be people with higher education were more conscious and thus were coming to hospitals for testing.

Among COVID-19 suspected healthcare workers from our surveillance hospitals, one out of four was SARS-CoV-2 infected (27%). Chartterjee et. al reported that 5% of symptomatic HCWs were SARS-COV-2 positive in India.[26] This was not a surprise as healthcare workers remain vulnerable to infectious disease in any low- and middle-income countries (LMICs) such as Bangladesh and demand adequate preparedness to fight against COVID-19.[27] Our findings also support that HCWs were getting infected at a much higher rate than India and, even more than that of a COVID-19 dedicated tertiary care hospital in Dhaka (11%),[28] Bangladesh. Thereby, appropriate measures should be taken to prevent primary infection from patients and secondary infection from colleagues. Appropriate measures such as Infection Prevention and Control training, adequate PPE supply, and their proper use should be taken into consideration with high priority to protect HCWs from getting infected from their workplace.

The positivity rate helps public health officials to assess the disease burden at different time point. COVID-19 positivity rate among the tested patients was increasing till July, followed by a gradual decline, similar to the country trend as reported by the Director General of Health Services (DGHS) Bangladesh and World Health Organization report.[29,30] There was a sharp drop in specimen collection in the first week of August due to "Eid holidays" the biggest religious festival for Muslims.

During the initial days of the COVID-19 crisis, there was a deficiency of adequate data to make appropriate policy decisions for Bangladesh.[31] Providing timely test reports and feeding peripheral sites' data from our surveillance hospitals to the government recording system greatly enhanced the management of the novel coronavirus crisis. Moreover, our work generated some key information about the ongoing COVID-19 pandemic in Bangladesh. COVID-19 suspected patients were found more at OPD than inpatient department, indicating that patients with COVID-19 symptoms were primarily mild, thereby seeking treatment from the OPD. Clinical features widely vary from asymptomatic infection (40% to 45% of SARS-CoV-2 infections) to death from acute respiratory distress syndrome (ARDS).[5,6,32] Chinese researchers reported fever, cough, and expectoration were the commonest symptoms[33] in a multi-centered study. Another meta-analysis[34] revealed fever (88.7%), cough (57.6%), and dyspnea (45.6%) were the prominent presentation. We found cough followed by fever as the top two presenting symptoms of COVID-19 patients. Additionally, sore throat, loss of taste and loss of smell, headache, muscle& joint pain were more likely to occur among laboratory-confirmed COVID-19 patients. Nothing conclusive, but these differences could be used carefully by the treating physicians to manage a suspected COVID-19 patient initially before getting the lab report.

Comorbidities play a crucial role towards disease progression. Diabetes was the most commonly reported factor towards the adverse outcome of COVID-19 patients and their disease progression,[35] requiring more hospitalization in the ICU and associated with more death compared to non-diabetic COVID-19 patients.[36] Our surveillance data showed that diabetic patients were more susceptible to get a COVID-19 infection than others. So, besides other co-morbidities such as cardiovascular diseases, clinicians should consider additional clinical measures to manage a COVID-19 positive diabetic patient.

Mortality rate is one of the key indicators in public health. Our surveillance data revealed that the percentage of death among our COVID-19 positive patients was a little higher (2.3%), than the global average death rate (2.2%) as of 22nd March 2021.[2] This death rate was possible to capture due to the unique post-discharge telephone follow up of enrolled patients after 30 days of enrollment for their outcome. Among all COVID-19 positive patients identified through the surveillance, we detected only 28% death from the surveillance hospitals, the remaining 72% deaths were possible to capture from this unique follow-up strategy of our sentinel surveillance system.

We observed, elderly, co-morbidity, having breathing difficulty, smoking, and admission in the inpatient department due to more severe illness were more likely to be the risk factors for death among the SARS-CoV-2 infected patients. Regarding gender, Italy reported more death among men than women.[37] Nationally, Bangladesh has more COVID-19 deaths among men (76%) than women (24%),[38] but we did not find any significant difference in death rate between males and females from our surveillance. A nationwide analysis in China showed that age between 65 and 74 years, coronary heart disease, cerebrovascular disease, dyspnea were independent risk factors associated with fatal outcome.[39] China CDC analyzed 44,000 COVID patients' data and reported elderly, diabetes, cardiovascular disease, hypertension and chronic respiratory disease were all associated with an increased risk of death.[40] In the United Kingdom, people aged over 70 years with cardiovascular and respiratory diseases were considered as high-risk group.[41] Smoking was associated with increased risks of COVID-19 death and disease progression, a finding similar to other studies.[42–45] The WHO also mentioned increased severity of disease and mortality in hospitalized COVID-19 patients among smokers.[46] One meta-analysis reported a pooled OR of 1.89 (95% CI: 1.10-3.24) on the severity of this disease among smokers than non-smokers.[44] Another systematic review reported a significant association between smoking and the progression of COVID-19 (OR: 1.91; 95% CI: 1.42-2.59); the authors commented that the actual risk of smoking might be higher.[47] Thereby, for a better outcome from COVID-19 infection during this pandemic smoking should be avoided. The surveillance data also showed more deaths occurred among critically ill hospitalized patients, which is natural. Thereby, an improved referral system from a district-level hospital to a tertiary level or specialized hospital could be considered for high-risk patients, which might reduce mortality.

Despite all efforts, our work had certain limitations. Based on our available resources and government priority, we conducted this surveillance at only four hospitals in different locations and enrolled suspected patients for three months only, with an additional one-month follow-up period. Thus, our findings might not be generalized for the whole Bangladeshi population. Moreover, we might have missed the true prevalence of COVID-19 patients as we did not screen any asymptomatic patients. We only reported hospital-based prevalence because it was beyond the scope of this platform to estimate the community burden of COVID-19 in Bangladesh.

## Conclusion

Of the patients attending the surveillance hospitals with COVID-19 symptoms during the reporting period, more than one-third had a laboratory-confirmed COVID-19 and, this was more common among outpatients with peak positivity in July. Elderly population, shortness of breath, co-morbid condition, smoking history, severe illness requiring hospital treatment were identified as the factors associated with death among COVID-19 patients. Policymakers may consider a system for the early identification of the COVID-19 positive individuals at high risk to provide special care with time appropriate treatment. Our effort strengthened government's capacity for rapid case detection, reporting, and quick containment efforts. Continuing this sentinel surveillance platform can better characterize disease patterns in populations over time, thus support the government by assessing the magnitude of the health problem and developing a data-driven effective management strategy as well as can monitor the progress towards the reduction of COVID-19 cases after vaccination campaign for SARS-CoV-2.

**Contributors:** The study concept was developed by FC and PD. The protocol was drafted by PD and critically revised by FC, SB, MR (Mahmudur Rahman), MR (Mahbubur Rahman), AA, TS, and MF. Data extraction and quality assessment was performed by ZA, SM AI and PD. Laboratory aspect was managed by ZR and MR (Mustafizur Rahman). PD developed the first draft manuscript. MR (Mahbubur Rahman), MB, SB, and all other authors provided feedback for all sections of the protocol including the design, analysis and revising the manuscript. All authors have approved the final version of the manuscript.

**Data availability statement:** Data cannot be made publicly available because these are confidential. Data are available from the respective department of icddr,b (www.icddrb.org) for researchers who meet the criteria for access to confidential data.

**Data sharing statement:** No additional data available.

**Disclaimer:** Our funding sources had no role in the design of the protocol, and was not involved during the methodological execution, data analyses and interpretation and decision to submit or to publish the study results.

**Patient and public involvement:** Due to the design of this study, it was not appropriate to involve patients and/or the public themselves in the design, or conduct, or reporting, or dissemination plans of this research.

**Ethics statements:** The protocol was reviewed and approved by the institutional review boards (IRB; Research Review Committee and Ethical Review Committee) of the International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b). We obtained written, informed consent of the participants before enrollment.

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**Table 1.** Socio-demographic characteristics of suspected COVID-19 patients in selected hospitals of Bangladesh, June-August 2020

| Characteristics | | Suspected COVID-19 patients (N=2345) | SARS-CoV-2 Positive by rRT-PCR | | |
|---|---|---|---|---|---|
| | | | Total Positive (922) | Inpatient (57) n (%) | Out-patient (865) n (%) |
| Age (in years) | | | | | |
| | Median (IQR) | 35 (26-48) | 38 (30-50) | 55 (45-69) | 38 (29-48) |
| Age sub-groups | | | | | |
| | 0-5 | 25 (1.11) | 6 (0.7) | 1 (1.7) | 5 (0.6) |
| | 6-10 | 30 (1.3) | 11 (1.2) | 0 (0) | 11 (1.3) |
| | 11-20 | 167 (7.1) | 42 (4.5) | 0 (0) | 42 (4.8) |
| | 21-30 | 684 (29.1) | 228 (24.7) | 5 (8.7) | 223 (25.8) |
| | 31-40 | 594 (25.3) | 246 (26.6) | 6 (10.5) | 240 (27.7) |
| | 41-50 | 382 (16.3) | 182 (19.7) | 11 (19.3) | 171 (19.7) |
| | 51-60 | 267 (11.4) | 125 (13.5) | 8 (14.0) | 117 (13.5) |
| | 60+ | 196 (8.3) | 82 (8.8) | 26 (45.6) | 56 (6.5) |
| Sex | | | | | |
| | Male | 1590 (67.8) | 654 (70.9) | 38 (66.7) | 616 (71.2) |
| Occupation | | | | | |
| | HCW | 302 (12.9) | 83 (9.0) | 2 (3.5) | 81 (9.4) |
| | Service | 946 (40.3) | 431 (46.8) | 7 (12.3) | 424 (49.0) |
| | Business | 154 (6.6) | 82 (8.9) | 6 (10.5) | 76 (8.8) |
| | Student | 223 (9.5) | 68 (7.4) | 0 (0) | 68 (7.9) |
| | Dependent | 215 (9.1) | 73 (7.9) | 22 (38.6) | 51 (5.9) |
| | Unemployed | 145 (6.1) | 64 (6.9) | 9 (15.8) | 55 (6.3) |
| | Others* | 360 (15.3) | 121 (13.1) | 11 (19.3) | 110 (12.7) |

| Education (years) | | | | |
|---|---|---|---|---|
| No formal schooling | 155 (6.6) | 44 (4.8) | 11 (19.3) | 33 (3.8) |
| 1-5 | 255 (10.9) | 89 (9.7) | 11 (19.3) | 78 (9.0) |
| 6-10 | 496 (21.2) | 178 (19.3) | 22 (38.6) | 156 (18.0) |
| 11-12 | 367 (15.7) | 144 (15.6) | 7 (12.3) | 137 (15.8) |
| >12 | 1072 (45.6) | 467 (50.7) | 6 (10.5) | 461 (53.4) |

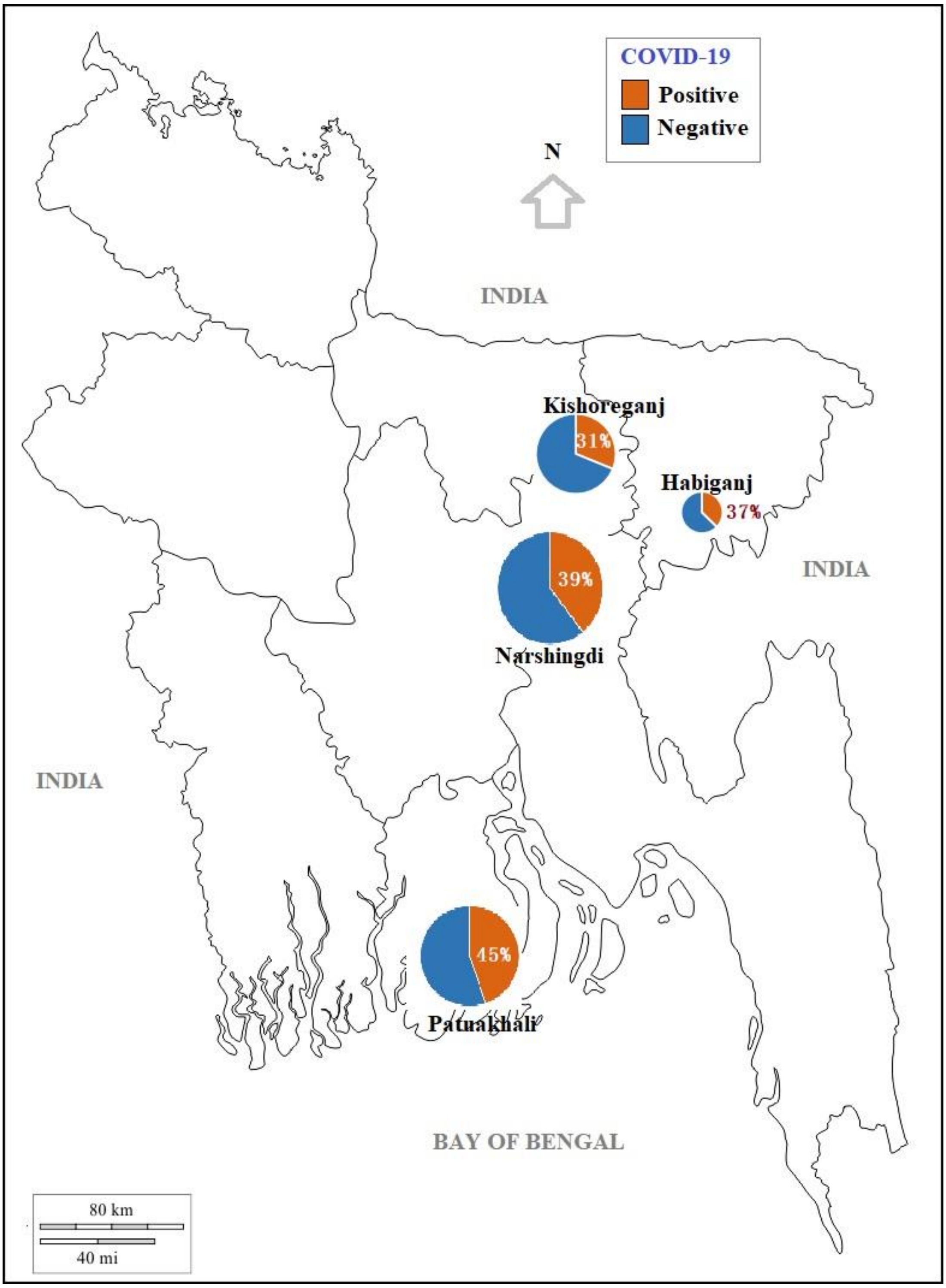
**Farmer, day-labour, small shop owner, rickshaw/van puller, driver etc.*

**Table 2.** Factors associated with adverse outcome (death) among COVID-19 positive patients in selected hospitals of Bangladesh, June-August 2020.

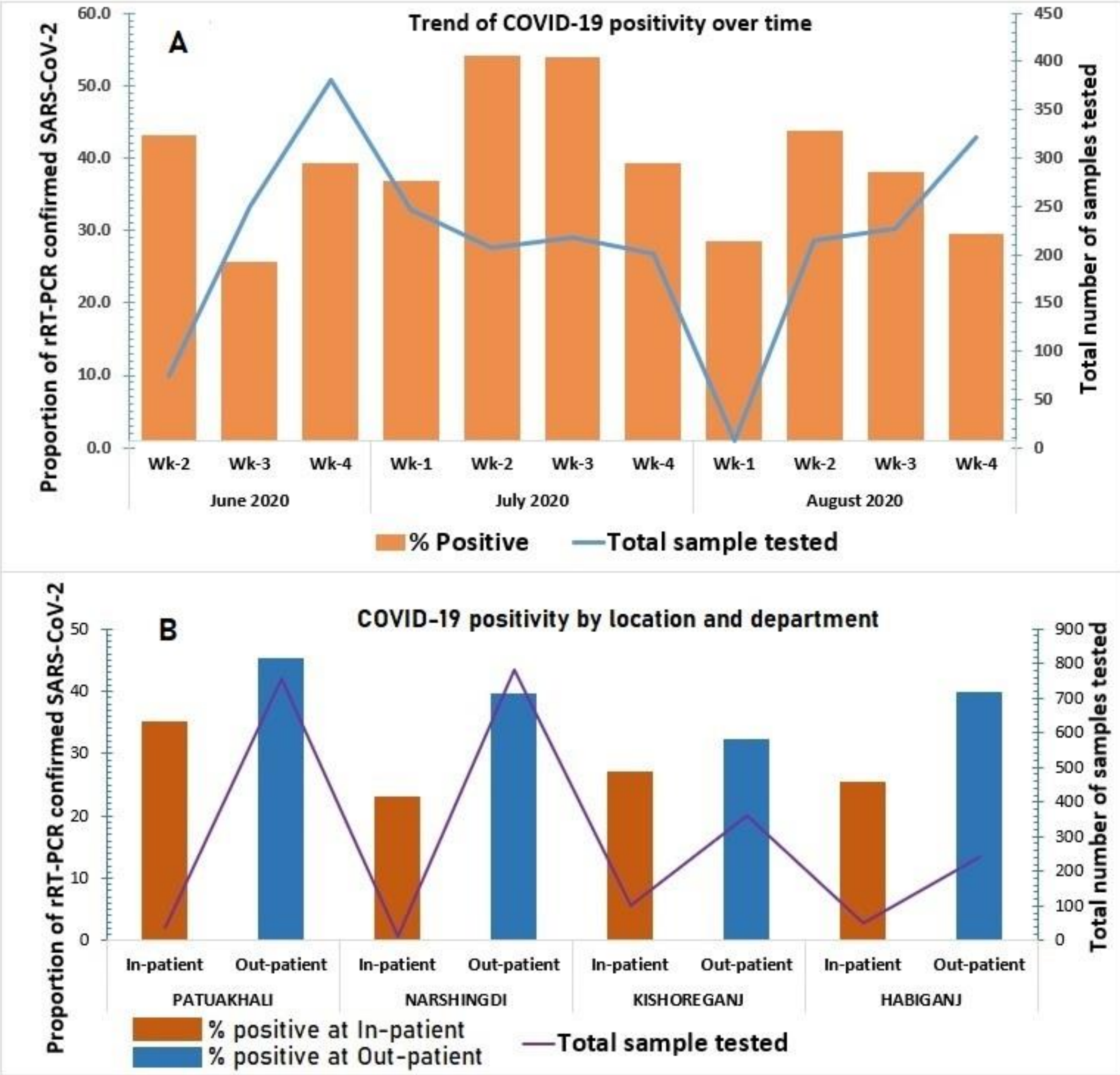
| Factors | | Frequency N=922 | Death n=21 Frequency (%) | Odds ratio OR (95% CI) | Adjusted odds ratio AOR (95% CI) |
|---|---|---|---|---|---|
| Age* | 0-59 years | 812 | 8 (1%) | 1 | 1 |
| | ≥ 60 years | 110 | 13 (11.8%) | 13.5 (5.4-33.3) | 13.9 (5.5-34.5) |
| Sex | Male | 654 | 14 (2.1%) | 1 | 1 |
| | Female | 268 | 7 (2.6%) | 1.2 (0.5-3.0) | 1.5 (0.55-4.0) |
| Health care worker | Yes | 83 | 0 (0%) | 1 | 1 |
| | No | 839 | 21 (2.5%) | - | - |
| Symptoms | ≤3 symptoms | 314 | 7 (2.2%) | 1 | 1 |
| | >3 symptoms | 608 | 14 (2.3%) | 1.0 (0.4-2.5) | 1.4 (0.52-3.9) |
| Shortness of breath* | No | 700 | 4 (0.6%) | 1 | 1 |
| | Yes | 222 | 17 (7.7%) | 14.4 (4.8-43) | 9.7 (3.0-30.4) |
| Comorbidity* | No | 538 | 2 (0.4%) | 1 | 1 |
| | Yes | 384 | 19 (4.9%) | 13.9 (3.2-60) | 4.8 (1.05-21.7) |
| History of smoking | No | 812 | 14 (1.7%) | 1 | 1 |
| | Yes | 110 | 7 (6.4%) | 3.9 (1.5-9.8) | 2.2 (0.71-7.1) |
| Treatment received* | OPD | 865 | 12 (1.4%) | 1 | 1 |
| | inpatient | 57 | 9 (15.8%) | 13.3 (5.3-33) | 3.4 (1.2-9.8) |

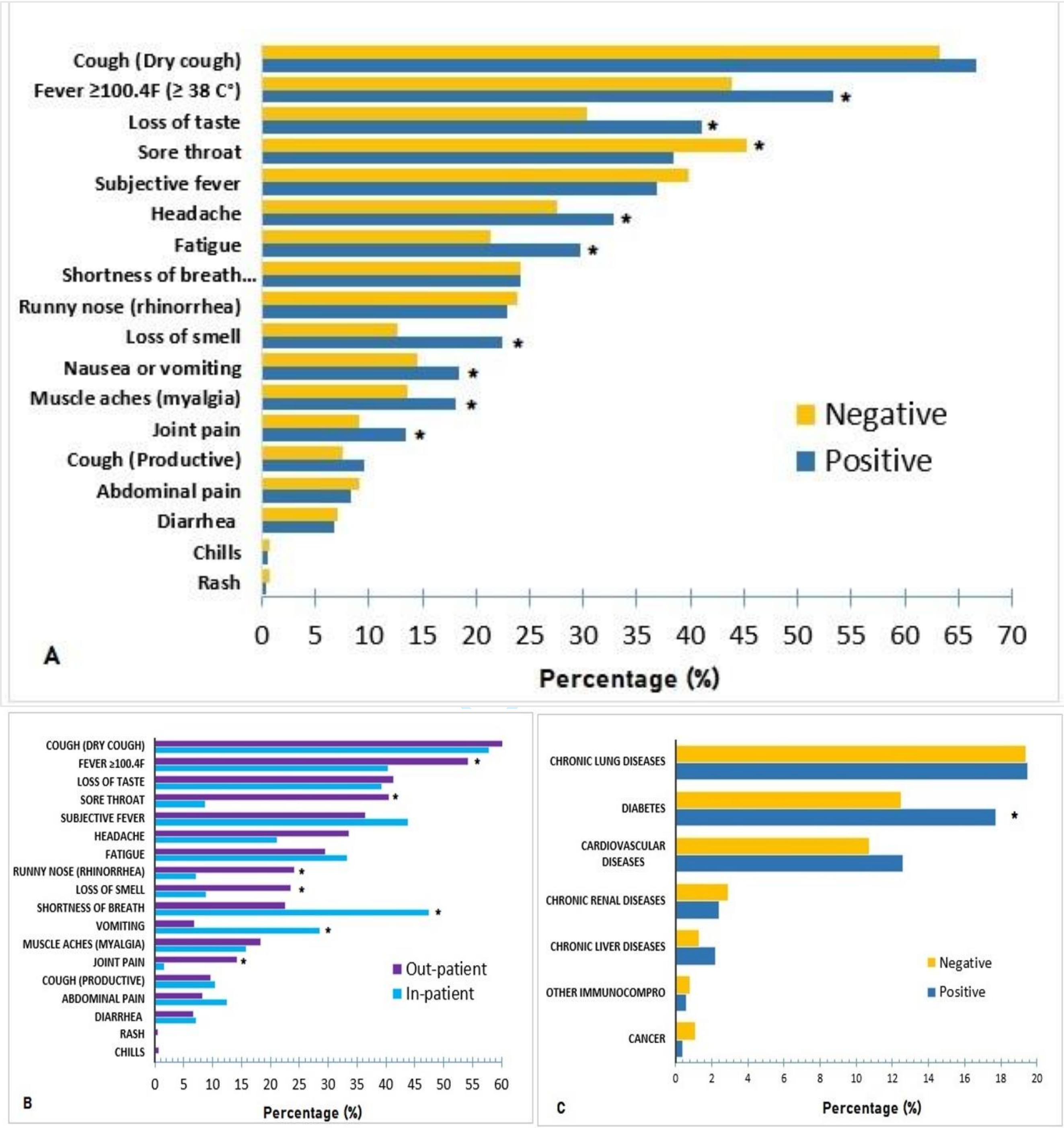
| | | | | | |
|---|---|---|---|---|---|
| Duration of hospital attendance from the onset of symptom* | ≥ 2 days | 880 | 17 (1.9%) | 1 | 1 |
| | < 2 days | 42 | 4 (9.8%) | 5.4 (1.8-17.1) | 4.7 (1.2-17.8) |

***Factors with a significant difference between groups***



COVID-19
Positive
Negative
N
INDIA
Kishoreganj
31%
Habiganj
37%
INDIA
39%
Narshingdi
INDIA
45%
Patuakhali
BAY OF BENGAL
80 km
40 mi


A
Trend of COVID-19 positivity over time
Proportion of rRT-PCR confirmed SARS-CoV-2
Total number of samples tested
60.0
50.0
40.0
30.0
20.0
10.0
0.0
450
400
350
300
250
200
150
100
50
0
Wk-2
Wk-3
Wk-4
Wk-1
Wk-2
Wk-3
Wk-4
Wk-1
Wk-2
Wk-3
Wk-4
June 2020
July 2020
August 2020
% Positive
Total sample tested
B
COVID-19 positivity by location and department
Proportion of rRT-PCR confirmed SARS-CoV-2
Total number of samples tested
50
40
30
20
10
0
900
800
700
600
500
400
300
200
100
0
In-patient
Out-patient
In-patient
Out-patient
In-patient
Out-patient
In-patient
Out-patient
PATUAKHALI
NARSHINGDI
KISHOREGANJ
HABIGANJ
% positive at In-patient
% positive at Out-patient
Total sample tested


Cough (Dry cough)
Fever ≥100.4F (≥ 38 C°)
Loss of taste
Sore throat
Subjective fever
Headache
Fatigue
Shortness of breath...
Runny nose (rhinorrhea)
Loss of smell
Nausea or vomiting
Muscle aches (myalgia)
Joint pain
Cough (Productive)
Abdominal pain
Diarrhea
Chills
Rash
Negative
Positive
0 5 10 15 20 25 30 35 40 45 50 55 60 65 70
Percentage (%)
A
COUGH (DRY COUGH)
FEVER ≥100.4F
LOSS OF TASTE
SORE THROAT
SUBJECTIVE FEVER
HEADACHE
FATIGUE
RUNNY NOSE (RHINORRHEA)
LOSS OF SMELL
SHORTNESS OF BREATH
VOMITING
MUSCLE ACHES (MYALGIA)
JOINT PAIN
COUGH (PRODUCTIVE)
ABDOMINAL PAIN
DIARRHEA
RASH
CHILLS
Out-patient
In-patient
0 5 10 15 20 25 30 35 40 45 50 55 60
Percentage (%)
B
CHRONIC LUNG DISEASES
DIABETES
CARDIOVASCULAR DISEASES
CHRONIC RENAL DISEASES
CHRONIC LIVER DISEASES
OTHER IMMUNOCOMPRO
CANCER
Negative
Positive
0 2 4 6 8 10 12 14 16 18 20
Percentage (%)
C

**Supplementary table 1**. Distribution of deaths among COVID-19 positive patients in selected hospitals of Bangladesh, June-August 2020.

| | Hospital death n= 16 | | Home death n=5 | |
|---|---|---|---|---|
| **Age (years)** | | | | |
| Lowest, highest | 40, 85 | | 51, 90 | |
| Median (IQR) | 65 (55-69) | | 64 (52-70) | |
| **Sex** | | | | |
| Male | 11 (69) | | 3 (60) | |
| **Timing of death from symptom onset** | | | | |
| 0-7 days | 6 (38) | 6 (38) Cum. | 3 (60) | 3 (60) Cum. |
| 8-15 days | 9 (56) | 15 (94) | 2 (40) | 5 (100) |
| 16-40 days | 1 (6) | 16 (100) | | |
| **Manner of death** | | | | |
| Disease | 16 | | 5 (100) | |
| Accident | 0 | | 0 | |
| Sudden death (heart attack) | 0 | | 0 | |
| **Comorbidity present (anyone)** | 15 (94%) | | 4 (80) | |
| DM | 9 (56) | | 2 (40) | |
| Asthma/COPD | 4 (25) | | 2 (40) | |
| Heart disease/HTN | 6 (37) | | 2 (40) | |
| Chronic renal disease | 4 (25) | | 0 | |
| Cancer (uterine) | 1 (6) | | 0 | |
| **Clinical course of treatment** | | | | |
| Oxygen required | 16 (100) | | 3 (60) [ 2 got oxygen at home] | |
| ICU admitted | 3 (19) | | | |
| CCU admitted | 1 (6) | | | |
| Dialysis required | 1 (6) | | | |
| **Cause of death as stated from hospital as reported** | | | | |
| COVID-19 + Respiratory failure | 14 (88) | | | |
| Pneumonia | 1 (6) | | | |
| Chronic renal failure | 1 (6) | | | |

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

| | Item No | Recommendation | Page No |
|---|---|---|---|
| **Title and abstract** | 1 | (*a*) Indicate the study's design with a commonly used term in the title or the abstract | 1 |
| | | (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found | 1 |
| **Introduction** | | | |
| Background/rationale | 2 | Explain the scientific background and rationale for the investigation being reported | 4-5 |
| Objectives | 3 | State specific objectives, including any prespecified hypotheses | 5 |
| **Methods** | | | |
| Study design | 4 | Present key elements of study design early in the paper | 6 |
| Setting | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | 6-7 |
| Participants | 6 | (*a*) Give the eligibility criteria, and the sources and methods of selection of participants | 6 |
| Variables | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable | 8 |
| Data sources/ measurement | 8* | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group | *NA* |
| Bias | 9 | Describe any efforts to address potential sources of bias | NA |
| Study size | 10 | Explain how the study size was arrived at | NA |
| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why | 7 |
| Statistical methods | 12 | (*a*) Describe all statistical methods, including those used to control for confounding | 7 |
| | | (*b*) Describe any methods used to examine subgroups and interactions | 7 |
| | | (*c*) Explain how missing data were addressed | NA |
| | | (*d*) If applicable, describe analytical methods taking account of sampling strategy | |
| | | (*e*) Describe any sensitivity analyses | |
| **Results** | | | |
| Participants | 13* | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed | 8 |
| | | (b) Give reasons for non-participation at each stage | NA |
| | | (c) Consider use of a flow diagram | NA |
| Descriptive data | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders | 8-9 |
| | | (b) Indicate number of participants with missing data for each variable of interest | NA |
| Outcome data | 15* | Report numbers of outcome events or summary measures | 7-10 |
| Main results | 16 | (*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included | 10 |

| | | | |
|---|---|---|---|
| | | (*b*) Report category boundaries when continuous variables were categorized | NA |
| | | (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period | |
| Other analyses | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses | NA |
| **Discussion** | | | |
| Key results | 18 | Summarise key results with reference to study objectives | 10-15 |
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias | 15 |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence | 16 |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results | 15 |
| **Other information** | | | |
| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based | 16 |

*Give information separately for exposed and unexposed groups.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

# Establishing a sentinel surveillance system for the novel coronavirus disease 2019 (COVID-19) in a resource limited county: methods, system attributes and early findings

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| Secondary Subject Heading: | Epidemiology, Global health, Infectious diseases |
| Keywords: | COVID-19, Epidemiology < TROPICAL MEDICINE, Public health < INFECTIOUS DISEASES, Diagnostic microbiology < INFECTIOUS DISEASES, EPIDEMIOLOGY |
| | |

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# Establishing a sentinel surveillance system for the novel coronavirus disease 2019 (COVID-19) in a resource limited county: methods, system attributes and early findings

Pritimoy Das[1,†], Zubair Akhtar[1], Syeda Mah-E-Muneer[1], Md Ariful Islam[1], Mohammed Ziaur Rahman[1], Mustafizur Rahman[1], Mahmudur Rahman[1], Mahbubur Rahman[2], Mallick Masum Billah[2], ASM Alamgir[2], Meerjady Sabrina Flora[2], Tahmina Shirin[2], Sayera Banu[1], Fahmida Chowdhury[1]

[1]Infectious Diseases Division, International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b), Dhaka, Bangladesh
[2]Institute of Epidemiology, Disease Control and Research (IEDCR), Dhaka, Bangladesh

[†]Correspondence to Pritimoy Das; pritimoydas@gmail.com



## ABSTRACT

**Objectives** To establish a hospital-based platform to explore the epidemiological and clinical characteristics of patients screened for COVID-19.

**Design** Hospital-based surveillance.

**Setting** This study was conducted in four selected hospitals in Bangladesh during 10th June to 31st August 2020.

**Participants** In total, two thousand three hundred and forty-five patients of all age (68% male) attending the outpatient and inpatient departments of surveillance hospitals with any one or more of the following symptoms within last 7 days- fever, cough, sore throat, and respiratory distress.

**Outcome measures** The outcome measures were COVID-19 positivity and mortality rate among enrolled patients. Pearson's $\chi^2$ test was used to compare the categorical variables (sign-symptoms, co-morbidities, admission status and COVID-19 test results). Regression analysis was performed to determine the association between potential risk factors and death.

**Results** COVID-19 was detected among 922 (39%) enrolled patients. It was more common in outpatients with a peak positivity in 2nd week of July (112, 54%). The median age of the confirmed COVID-19 cases was 38 years (IQR: 30-50), 654 (71%) were male, and 83 (9%) were healthcare workers. Cough (615, 67%) was the most common symptom, followed by fever (493, 53%). Diabetic patients were more likely to get COVID-19 than non-diabetic (48% vs. 38%; OR:1.5; 95% CI:1.2-1.9). The death rate among COVID-19 positive was 2.3%, n=21. Death was associated with age ≥ 60 years (AOR:13.9; 95% CI:5.5-34), shortness of breath (AOR:9.7; 95% CI: 3.0-30), co-morbidity (AOR:4.8; 95% CI:1.1-21.7), smoking history (AOR: 2.2, 95% CI:0.7-7.1), attending the hospital in <2 days of symptom onset due to critical illness (AOR: 4.7; 95% CI:1.2-17.8) and hospital admission (AOR:3.4; 95% CI: 1.2-9.8).

**Conclusions** COVID-19 positivity was observed in more than one-third of suspected COVID-19 patients attending selected hospitals. While managing such patients, the risk factors identified for higher death rates should be considered.

**Key words:** Bangladesh, COVID-19, hospital-based study, SARS-CoV-2, sentinel surveillance.

## Strengths and limitations of this study

- The sentinel surveillance for COVID-19 was implemented in collaboration with a government public health institution and an international research organization in resource-constrained settings.
- This was a multicentre study with representative hospitals included from almost all major administrative regions of Bangladesh.
- Our surveillance method was unique as we shared test results with patients at earliest and considered follow-up at 30-day after enrollment to track the prognosis of COVID-19 positive patients even after they were discharged from the enrolling hospital.
- As we did not test any asymptomatic patients and community burden estimation was beyond our scope, the true prevalence of COVID-19 patients might be higher than reported in our study.

## Introduction

Starting from its inception at Wuhan, Hubei Province, China, the novel coronavirus named severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has spread across the world within a few months, causing Coronavirus Disease 2019 (COVID-19).[1] Globally, 129,651,305 cases and 2.8 million deaths were recorded till 31th March 2021.[2] This virus manifests various clinical characteristics, from asymptomatic infection to severe pneumonia, vasculitis, and death.[3–6] It was declared a public health emergency of international concern (PHEIC) by the world health organization (WHO) in 30th January 2020 and subsequently a pandemic on 11th March 2020.[7] During that early stage of this coronavirus disease, there was uncertainty and variation regarding the epidemiological, clinical, and virological characteristics of this novel infectious disease. Though COVID-19 cases were reported from 198 countries or regions, and over 400,000 people were confirmed to be infected globally (24th March 2020),[8] its transmission dynamics within the human population was unclear, so WHO designed a protocol for the countries to investigate the COVID-19 outbreaks locally and emphasized COVID-19 surveillance to understand the country situation.[9]

Bangladesh, a country in Southeast Asia, exhibited different epidemiological features compared to other countries regarding the influenza virus in terms of seasonality, severity, and mortality.[10,11] On 8th March 2020, the first three cases of confirmed COVID-19 were reported in Bangladesh,[12] and subsequently, the number of confirmed cases and deaths increased: at the end of the first month, there were 51 confirmed cases with five deaths from COVID-19.[13] As COVID-19 was a novel virus, there was minimal information regarding its severity and magnitude in Bangladesh.

The government of Bangladesh (GoB) initiated several efforts for the early detection of the virus to mitigate the spread such as screening of passengers at airports, land ports, and maritime ports; hotline system to notify any suspected case of COVID-19 to the Institute of

Epidemiology, Disease Control and Research (IEDCR) so that their specimens could be collected and tested. Moreover, passengers arriving from countries with COVID-19 outbreaks were screened at the point of entries (PoE) and monitored for any symptom onset for 14 days, considering the virus's incubation period recommended by the WHO.[14] However, these efforts were not enough to detect COVID-19 patients, as asymptomatic COVID-19 carriers already unfolded in their community and spread the virus in different geographical locations across Bangladesh.[15] Patients with COVID-19 symptoms were reported from different hospitals and needed to be tested for diagnosis and appropriate treatment purposes.[16] Initially, there were 10 laboratories in capital Dhaka city and five laboratories outside Dhaka had COVID-19 testing facility in Bangladesh.[17] Thus, as a part of the pandemic preparedness and responses, there was an immediate need to establish a hospital-based platform to screen suspected COVID-19 patients to support GoB in hospitals where PCR-based COVID-19 testing facility was not available. The GoB initiated a countrywide system for detecting COVID-19 cases by prioritizing divisional hospitals, medical college hospitals, and few specialized hospitals to screen and test for COVID-19. Moreover, there was a knowledge gap on clinical and epidemiological data of COVID-19 patients in Bangladesh during the first wave of the pandemic from any sentinel sites involving multiple public and private hospitals across the country.

The quality of surveillance data in many developing countries is hampered by a variety of factors, including a lack of resources and training.[18] Ibrahim et al. (2020) looked into various COVID-19 surveillance activities around the world and categorized them into a systematic review paper of thirty articles.[19] Our surveillance falls into a combination of sentinel surveillance and enhanced surveillance of hospitalized cases in which risk groups can be identified, tested, and followed up on via a hospital and laboratory network. Current surveillance included searching for suspected COVID-19 patients among hospitalized patients as well as screening and testing patients from outpatient. In Singapore, a similar approach was taken for the investigation and confinement efforts for COVID-19.[20,21]

To support the containment efforts for COVID-19, the International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b) and the Institute of Epidemiology, Disease Control and Research (IEDCR) under the Bangladesh Ministry of Health and Family Welfare jointly conducted this surveillance in selected hospitals where there was no nearby PCR based COVID-19 testing facility. The aim of this study was to establish a hospital-based platform to describe and analyze epidemiological and clinical characteristics of patients screened for COVID-19 in selected Bangladeshi hospitals with limited resources during the first wave of COVID-19 pandemic of the pandemic.

## Methods

### *Setting*

The surveillance was conducted at the outpatient department (OPD) and inpatient department (IPD) of four selected hospitals where patients sought healthcare with suspected COVID-19 symptoms. There were three public hospitals and one private hospital, all of which were in different geographical locations across Bangladesh **(Figure 1)**. The public hospitals namely Sadar Hospital, Hobiganj (24°22'24.77", 91°25'3.62"), General Hospital, Potuakhali (22°21'52.19", 90°19'37.25" and District Hospital, Narshingdi (23°55' 48.6", 90°42' 9.84"), all having 100-250 number of beds. Jahurul Islam Medical College hospital, Kishoregonj (24°12' 2.26", 90°55'1.81") is a general tertiary level 500 bed teaching hospital. To select these hospitals, we evaluated the ongoing national hospital-based Influenza surveillance platforms to identify the hospitals where there was no in-hospital or nearby polymerase chain reaction (PCR) based COVID-19 testing facility at that time but a high load of potential suspected COVID-19 patients in that geographical location. It was considered that additional support to these hospitals would strengthen COVID-19 case identification and reporting at the national level with generation of epidemiological data.

***Patient enrolment***

Within three months of the first COVID-19 case detection in the country, we deployed two trained field staff in each selected hospital (total eight field staff placed in four hospitals) for screening suspected COVID-19 patients among all the patients attending the fever clinic at OPD and among all inpatients admitted into the specific wards (medicine ward, pediatric ward, intensive care unit (ICU) and COVID-19 isolation ward). These field staffs worked with hospital physicians to enroll suspected COVID-19 patients.

Case-definition: Field staff actively screened for suspected COVID-19 patients using the following case definition: patient with any one or more of the following symptoms within last 7 days- fever, cough, sore throat, and respiratory distress. This case definition was applied by GoB to collect samples as suspected COVID-19 patient.

***Data collection***

After obtaining written informed consent from patients who met the suspected COVID-19 case definition, field staff collected data on socio-demographics (age, sex, occupation, educational level), travel history (local or international travel), and clinical characteristics (presenting symptoms, clinical signs, comorbidity, admission status, smoking history, duration of symptom onset to treatment seeking) from them. Field staff used proper personal protective equipment (PPE) such as N95 mask/medical mask, disposable gown, disposable cap, disposable gloves, face shield and goggles during data and specimen collection. Field staff used tablet computers to collect data syncing with local icddr,b server using mobile internet. This system allowed real-time monitoring of the situation across all hospitals by the research team centrally from Dhaka city. After 30 days of enrollment, the surveillance team (field staff, their supervisor and occasionally, the first author) followed up with each enrolled patient through mobile phone calls to register the outcome of their illnesses and updated the database accordingly. The outcome variables were COVID-19 positivity by RT-PCR test and the mortality among the SARS-CoV-2 infected patients.

***Specimen collection and Transportation***

Trained field staff collected a single nasopharyngeal swab through swab stick from each enrolled patients in viral transportation medium (VTM) and stored in a cool box between 2-4 °C temperature. Inhouse (icddr,b lab) VTM preparation was used for the collected samples. Every afternoon, a dedicated porter transported all the samples to icddr,b, Dhaka using a private car from three surveillance hospitals except Patuakhali. From Patuakhali, one of the dedicated porter brought samples to icddr,b by launch (public transport). All VTMs were handed over to icddr,b virology laboratory within 24 hours of specimen collection.

***Laboratory testing***

Nasopharyngeal swabs were tested for SARS-CoV-2 at the Virology Laboratory of icddr,b. Ribonucleic acid (RNA) was extracted from nasopharyngeal swab using QiaAmp Viral RNA Mini kit (Qiagen, Hilden, Germany). RNA was tested for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by real-time reverse transcription polymerase chain reaction (rRT-PCR) targeting SARS-CoV-2 specific ORF1ab- and N-gene. Any person with an rRT-PCR positive test result was defined as a laboratory-confirmed COVID-19 case/patient.

***Reporting to IEDCR, surveillance hospitals, and patients***

We received the laboratory test results on the following day of specimen collection. Our research team then shared the results with respective hospital authorities, district civil surgeons, divisional health directors, and the director of IEDCR over email. Moreover, we sent a text message (Short Message Service- SMS) to each enrolled patient informing their test report within 36 hours of specimen collection. Our investigators also responded to every query when any COVID-19 positive patient called them over the telephone upon getting the test result. The respective health care facilities then managed the patients following the existing government system.

### *Data analysis*

The data management and analysis were performed using the software Stata v.13 (Stata Corp LP, College Station, TX, USA). We summarized all categorical variables using frequency and percentage. We also summarized using mean and standard deviation (SD) for symmetrically distributed variables and median and interquartile range (IQR) for asymmetrically distributed variables. We performed Pearson's $\chi^2$ test to compare the categorical variables and considered $p<0.05$ as statistically significant. We used univariate logistic regression analysis for strengths of associations and identified risk factors for death, using odds ratio and adjusted for age and sex in the multivariable model.

### *Ethical consideration*

The protocol was reviewed and approved by the institutional review boards (IRB; Research Review Committee and Ethical Review Committee) of the International Centre for Diarrhoeal Disease Research, Bangladesh (Ref. number PR-20032). We obtained written, informed consent of the participants before enrollment. To ensure anonymity of the study participants and maintain the confidentiality, the names and identifying information of the participants was and will not be shared with anyone outside of the data collection team and this information was kept in locked cabinets and/or computers with passwords. Laboratory specimens were identified only by patient enrolment ID. Necessary permission was obtained from the respective hospitals before establishing the hospital-based platform and data collection.

***Patient and public involvement***

Patients or the public were not involved in the study design, or conduct, or reporting, or dissemination plans.

## Results

*COVID-19 positivity and Demographic characteristics*

During 10th June to 31st August 2020, we enrolled 2,345 suspected COVID-19 patients from four selected hospitals. Virology Laboratory of icddr,b tested all the 2,345 nasopharyngeal swab samples collected from these enrolled participants; of them, 922 (39.3%) were laboratory-confirmed COVID-19 patients. The median age of the confirmed COVID-19 patients was 38 years (Interquartile range, IQR: 30-50 years), and 654 (71%) were male. COVID-19 was mostly detected among patients aged between 21-40 years (474, 51.3%). About half of the COVID-19 positive patients (467, 50.7%) had a higher level of education (>12 years). We identified 302 (13%) of the patients meeting surveillance case definition were healthcare workers (HCW), and they constituted 83 (9%) of all confirmed COVID-19 patients **(Table 1)**.

*Seasonality and geographical variation*

Over the three months of the surveillance period, the peak of the COVID-19 positivity among suspected COVID-19 patients was detected in the 24th and 25th epi weeks (2nd and 3rd week of July 2020). We observed a relatively hard-to-reach riverside area (Patuakhali hospital) reporting the highest number and proportion of cases (355/793; 45%) compared to other hospitals in Narshingdi (313/796; 39%), Kishoreganj (144/462; 31%), and Habiganj (110/294; 37%). The proportion of test positivity over time dropped and gradually started declining from the epi week 28th (2nd week of August) (**Figure 1 and Figure 2 A, B**).

*Differences in clinical presentation between COVID-19 positive and COVID-19 negative patients*

The presenting clinical features in all suspected COVID-19 patients varied from dry cough (most common, 67%, n=1562) to rash (least common, 0.4%, n=9), (**Figure 3A**). We found fever ≥ 38◦ C (1252, 53% vs. 1077, 44%), loss of taste (964, 41% vs. 711, 30%), headache (772, 33% vs. 645, 27%), fatigue (696, 30% vs. 499, 21%), loss of smell (528, 23% vs. 295, 13%), nausea/vomiting (431, 18% vs. 340, 15%) and joint pain (314, 13% vs. 223, 9%) were more likely to be the presenting clinical features among COVID-19 positive patients compared to the negative patients (all $p<0.05$). On the other hand, though sore throat was a very common feature among suspected COVID-19 patients, it was less common in the COVID-19 positive patients than COVID-19 negative patients (900, 38% vs. 1060, 45%, $p=0.002$) (**Figure 3A**).

*IPD vs. OPD visits*

Most of the patients meeting the suspected COVID-19 case definition (2141, 91%) were identified from the outpatient departments of all the surveillance hospitals, and of them, 865 (40%) were COVID-19 positive. In contrast, among all patients enrolled from the inpatient departments, 57 (28%) were found COVID-19 positive. Shortness of breath (97, 47% vs. 482, 22%) and vomiting (58, 29% vs. 146, 7%) were more common clinical characteristics of COVID-19 positive patients admitted in the hospitals compared to COVID-19 patients who attended at outpatients (**Figure 3B**). However, fever (1163, 54% vs. 82, 40%), sore throat (869, 41% vs. 18, 9%), runny nose (518, 24% vs. 14, 7%), loss of smell (503, 24% vs. 18, 9%) and joint pain (304, 14% vs. 3, 2%) were more common clinical symptoms in COVID-19 patients at OPD compared to COVID-19 patients at IPD (All p values <0.05).

*Comorbidities among COVID-19 patients*

Compared to COVID-19 negative patients, patients with co-morbidities reported more infection with SARS-CoV-2, such as for chronic liver disease (20, 51% vs. 898, 39%), cardiovascular disease (116, 43% vs. 801, 39%), and diabetes (164, 48% vs. 755, 38%). Of these co-morbidities, diabetic patients showed significantly high susceptibility ($p < 0.05$) of getting infected with SARS-CoV-2 than non-diabetic patients (**Figure 3C**). Other than these co-morbidities, we also found 19 cancer patients meeting enrolment criteria; of them, four patients (21%) were COVID-19 positive; and among positive, one (25%) died.

*Mortality and associated risk factors*

Among the 922 laboratory-confirmed COVID-19 patients, 21 (2.3%) patients were reported dead from our routine follow-up after a month of enrolment. Of them, 76% (16/21) patients died at the same enrolment hospital or different hospitals, 24% (5/21) patients died at home or on the way to the hospital. From the onset of symptoms, 43% (9/21) of patients died within 7 days, and 95% (20/21) deaths occurred within 15 days (**Supplementary Table 1**). When we compared epidemiological factors for association with adverse outcome of their clinical progression, our data showed that death was more likely to occur among patients presenting with age ≥ 60 years (AOR:13.9; 95% CI: 5.5-34.5), shortness of breath (AOR:9.7; 95% CI: 3.0-30), co-morbidity (AOR:4.8; 95% CI: 1.1-21.7), smoking history (AOR:2.2, 95% CI: 0.7-7.1), attending to a hospital in <2 days from the onset of symptoms due to critical illness (AOR: 4.7; 95% CI: 1.2-17.8) and hospital admission (AOR:3.4; 95% CI: 1.2-9.8; **Table 2**).

## Discussion

Our hospital-based COVID-19 sentinel surveillance platform identified more than one-third (39%) of patients as laboratory-confirmed COVID-19 among the suspected COVID-19 patients attending the hospitals during the study period. This COVID-19 positivity rate was much higher to draw public health attention compared to WHO reported national data

(19.5%) from 8th March to 14th September 2020.[22] The national health system intended to collect specimens from symptomatic individuals, but considering resource constrain verification of symptoms was difficult and thereby some asymptomatic individuals could be included for testing. Moreover, people seeking a routine COVID-19 PCR test as a requirement for international travel was also included in the national system for COVID-19 reporting. In contrast, surveillance staff and physicians strictly verified the symptoms reported by each patient before enrolment and sample collection through the sentinel surveillance platform. This sentinel surveillance was strictly supervised and monitored by a team of dedicated researchers for the utmost quality of specimen and data collection from actual symptomatic patients and rapid transportation of specimens from remote field sites to central laboratory at Dhaka maintaining recommended standard temperature for rRT-PCR testing. Thereby, a robust sentinel COVID-19 surveillance is so important to better understand the actual disease burden in different administrative regions of a country.

More than half of our COVID-19 positive patients were young adults within the age group of 21-40 years. This was consistent (46.7%) with the WHO report for Bangladesh on morbidity and mortality weekly update (MMWU) as of 14th Sept 2020.[22] Among the COVID-19 positive patients, male was predominant. This was consistent with other nearby countries such as India, where researcher reported that male COVID-19 cases (65.39%) were more than females (34.61%).[23] This might be due to the male-dominant societies' unique health-seeking behavior like Bangladesh, where women do not seek healthcare unless severe.[24] This finding was similar (68% male) during March-April, the early phase of novel coronavirus detection in Bangladesh.[25] Other than male predominance, more than half of the COVID-19 positive patients were found to be educated for 12 years or more. This might not be the cause that educated people were more infected than less educated or uneducated; rather it may be people with higher education were more conscious and thus were coming to hospitals for testing.

Among COVID-19 suspected healthcare workers from our surveillance hospitals, one out of four was SARS-CoV-2 infected (27%). Chartterjee et. al reported that 5% of symptomatic HCWs were SARS-COV-2 positive in India.[26] This was not a surprise as healthcare workers remain vulnerable to infectious disease in any low- and middle-income countries (LMICs) such as Bangladesh and demand adequate preparedness to fight against COVID-19.[27] Our findings also support that HCWs were getting infected at a much higher rate than India and, even more than that of a COVID-19 dedicated tertiary care hospital in Dhaka (11%),[28] Bangladesh. Thereby, appropriate measures should be taken to prevent primary infection from patients and secondary infection from colleagues. Appropriate measures such as Infection Prevention and Control training, adequate PPE supply, and their proper use should be taken into consideration with high priority to protect HCWs from getting infected from their workplace.

The positivity rate helps public health officials to assess the disease burden at different time point. COVID-19 positivity rate among the tested patients was increasing till July, followed by a gradual decline, similar to the country trend as reported by the Director General of Health Services (DGHS) Bangladesh and World Health Organization report.[29,30] There was a sharp drop in specimen collection in the first week of August due to “Eid holidays” the biggest religious festival for Muslims.

During the initial days of the COVID-19 crisis, there was a deficiency of adequate data to make appropriate policy decisions for Bangladesh.[31] Providing timely test reports and feeding peripheral sites’ data from our surveillance hospitals to the government recording system greatly enhanced the management of the novel coronavirus crisis. Moreover, our work generated some key information about the ongoing COVID-19 pandemic in Bangladesh. COVID-19 suspected patients were found more at OPD than inpatient department, indicating that patients with COVID-19 symptoms were primarily mild, thereby seeking treatment from the OPD. Clinical features widely vary from asymptomatic infection (40% to 45% of SARS-CoV-2 infections) to death from acute respiratory distress syndrome (ARDS).[5,6,32] Chinese researchers reported fever, cough, and expectoration were the commonest symptoms[33] in a multi-centered study. Another meta-analysis[34] revealed fever (88.7%), cough (57.6%), and dyspnea (45.6%) were the prominent presentation. We found cough followed by fever as the top two presenting symptoms of COVID-19 patients. Additionally, sore throat, loss of taste and loss of smell, headache, muscle& joint pain were more likely to occur among laboratory-confirmed COVID-19 patients. Nothing conclusive, but these differences could be used carefully by the treating physicians to manage a suspected COVID-19 patient initially before getting the lab report.

Comorbidities play a crucial role towards disease progression. Diabetes was the most commonly reported factor towards the adverse outcome of COVID-19 patients and their disease progression,[35] requiring more hospitalization in the ICU and associated with more death compared to non-diabetic COVID-19 patients.[36] Our surveillance data showed that diabetic patients were more susceptible to get a COVID-19 infection than others. So, besides other co-morbidities such as cardiovascular diseases, clinicians should consider additional clinical measures to manage a COVID-19 positive diabetic patient.

Mortality rate is one of the key indicators in public health. Our surveillance data revealed that the percentage of death among our COVID-19 positive patients was a little higher (2.3%), than the global average death rate (2.2%) as of 22nd March 2021.[2] This death rate was possible to capture due to the unique post-discharge telephone follow up of enrolled patients after 30 days of enrollment for their outcome. Among all COVID-19 positive patients identified through the surveillance, we detected only 28% death from the surveillance hospitals, the remaining 72% deaths were possible to capture from this unique follow-up strategy of our sentinel surveillance system.

We observed, elderly, co-morbidity, having breathing difficulty, smoking, and admission in the inpatient department due to more severe illness were more likely to be the risk factors for death among the SARS-CoV-2 infected patients. Regarding gender, Italy reported more death among men than women.[37] Nationally, Bangladesh has more COVID-19 deaths among men (76%) than women (24%),[38] but we did not find any significant difference in death rate between males and females from our surveillance. A nationwide analysis in China showed that age between 65 and 74 years, coronary heart disease, cerebrovascular disease, dyspnea were independent risk factors associated with fatal outcome.[39] China CDC analyzed 44,000 COVID patients' data and reported elderly, diabetes, cardiovascular disease, hypertension and chronic respiratory disease were all associated with an increased risk of death.[40] In the United Kingdom, people aged over 70 years with cardiovascular and respiratory diseases were considered as high-risk group.[41] Smoking was associated with increased risks of COVID-19 death and disease progression, a finding similar to other studies.[42–45] The WHO also mentioned increased severity of disease and mortality in hospitalized COVID-19 patients among smokers.[46] One meta-analysis reported a pooled OR of 1.89 (95% CI: 1.10-3.24) on the severity of this disease among smokers than non-smokers.[44] Another systematic review reported a significant association between smoking and the progression of COVID-19 (OR: 1.91; 95% CI: 1.42-2.59); the authors commented that the actual risk of smoking might be higher.[47] Thereby, for a better outcome from COVID-19 infection during this pandemic smoking should be avoided. The surveillance data also showed more deaths occurred among critically ill hospitalized patients, which is natural.

Thereby, an improved referral system from a district-level hospital to a tertiary level or specialized hospital could be considered for high-risk patients, which might reduce mortality.

Despite all efforts, our work had certain limitations. Based on our available resources and government priority, we conducted this surveillance at only four hospitals in different locations and enrolled suspected patients for three months only, with an additional one-month follow-up period. Thus, our findings might not be generalized for the whole Bangladeshi population. Moreover, we might have missed the true prevalence of COVID-19 patients as we did not screen any asymptomatic patients. We only reported hospital-based prevalence because it was beyond the scope of this platform to estimate the community burden of COVID-19 in Bangladesh.

## Conclusion

Of the patients attending the surveillance hospitals with COVID-19 symptoms during the reporting period, more than one-third had a laboratory-confirmed COVID-19 and, this was more common among outpatients with peak positivity in July. Elderly population, shortness of breath, co-morbid condition, smoking history, severe illness requiring hospital treatment were identified as the factors associated with death among COVID-19 patients. Policymakers may consider a system for the early identification of the COVID-19 positive individuals at high risk to provide special care with time appropriate treatment. Our effort strengthened government's capacity for rapid case detection, reporting, and quick containment efforts. Continuing this sentinel surveillance platform can better characterize disease patterns in populations over time, thus support the government by assessing the magnitude of the health problem and developing a data-driven effective management strategy as well as can monitor the progress towards the reduction of COVID-19 cases after vaccination campaign for SARS-CoV-2.

**Contributors:** The study concept was developed by FC and PD. The protocol was drafted by PD and critically revised by FC, SB, MR (Mahmudur Rahman), MR (Mahbubur Rahman), AA, TS, and MF. Data extraction and quality assessment was performed by ZA, SM AI and PD. Laboratory aspect was managed by ZR and MR (Mustafizur Rahman). PD developed the first draft manuscript. MR (Mahbubur Rahman), MB, SB, and all other authors provided feedback for all sections of the protocol including the design, analysis and revising the manuscript. All authors have approved the final version of the manuscript.

**Data availability statement:** Data cannot be made publicly available because these are confidential. Data are available from the respective department of icddr,b (www.icddrb.org) for researchers who meet the criteria for access to confidential data.

**Data sharing statement:** No additional data available.

**Disclaimer:** Our funding sources had no role in the design of the protocol, and was not involved during the methodological execution, data analyses and interpretation and decision to submit or to publish the study results.

**Patient and public involvement:** Due to the design of this study, it was not appropriate to involve patients and/or the public themselves in the design, or conduct, or reporting, or dissemination plans of this research.

**Ethics statements:** The protocol was reviewed and approved by the institutional review boards (IRB; Research Review Committee and Ethical Review Committee) of the International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b). We obtained written, informed consent of the participants before enrollment.

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**Table 1.** Socio-demographic characteristics of suspected COVID-19 patients in selected hospitals of Bangladesh, June-August 2020

| Characteristics | | Suspected COVID-19 patients (N=2345) | SARS-CoV-2 Positive by rRT-PCR | | |
|---|---|---|---|---|---|
| | | | Total Positive (922) | Inpatient (57) n (%) | Out-patient (865) n (%) |
| Age (in years) | | | | | |
| | Median (IQR) | 35 (26-48) | 38 (30-50) | 55 (45-69) | 38 (29-48) |
| Age sub-groups | | | | | |
| | 0-5 | 25 (1.11) | 6 (0.7) | 1 (1.7) | 5 (0.6) |
| | 6-10 | 30 (1.3) | 11 (1.2) | 0 (0) | 11 (1.3) |
| | 11-20 | 167 (7.1) | 42 (4.5) | 0 (0) | 42 (4.8) |
| | 21-30 | 684 (29.1) | 228 (24.7) | 5 (8.7) | 223 (25.8) |
| | 31-40 | 594 (25.3) | 246 (26.6) | 6 (10.5) | 240 (27.7) |
| | 41-50 | 382 (16.3) | 182 (19.7) | 11 (19.3) | 171 (19.7) |
| | 51-60 | 267 (11.4) | 125 (13.5) | 8 (14.0) | 117 (13.5) |
| | 60+ | 196 (8.3) | 82 (8.8) | 26 (45.6) | 56 (6.5) |
| Sex | | | | | |
| | Male | 1590 (67.8) | 654 (70.9) | 38 (66.7) | 616 (71.2) |
| | Female | 755 (32.2) | 268 (29.1) | 19 (33.3) | 249 (28.8) |
| Occupation | | | | | |
| | HCW | 302 (12.9) | 83 (9.0) | 2 (3.5) | 81 (9.4) |
| | Service | 946 (40.3) | 431 (46.8) | 7 (12.3) | 424 (49.0) |
| | Business | 154 (6.6) | 82 (8.9) | 6 (10.5) | 76 (8.8) |
| | Student | 223 (9.5) | 68 (7.4) | 0 (0) | 68 (7.9) |
| | Dependent | 215 (9.1) | 73 (7.9) | 22 (38.6) | 51 (5.9) |
| | Unemployed | 145 (6.1) | 64 (6.9) | 9 (15.8) | 55 (6.3) |

| | | | | |
|---|---|---|---|---|
| Others* | 360 (15.3) | 121 (13.1) | 11 (19.3) | 110 (12.7) |
| Education (years) | | | | |
| No formal schooling | 155 (6.6) | 44 (4.8) | 11 (19.3) | 33 (3.8) |
| 1-5 | 255 (10.9) | 89 (9.7) | 11 (19.3) | 78 (9.0) |
| 6-10 | 496 (21.2) | 178 (19.3) | 22 (38.6) | 156 (18.0) |
| 11-12 | 367 (15.7) | 144 (15.6) | 7 (12.3) | 137 (15.8) |
| >12 | 1072 (45.6) | 467 (50.7) | 6 (10.5) | 461 (53.4) |

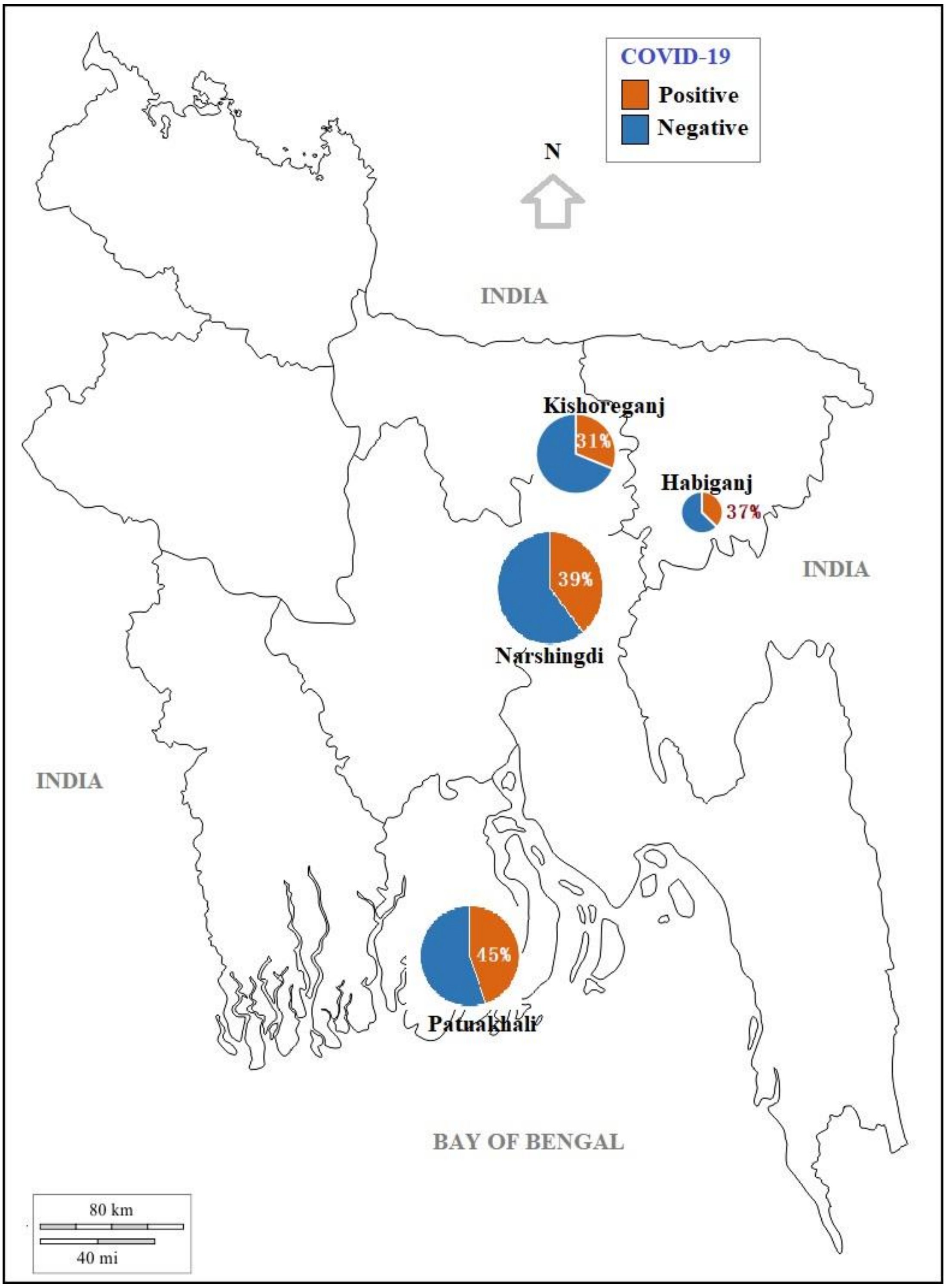
**Farmer, day-labour, small shop owner, rickshaw/van puller, driver etc.*

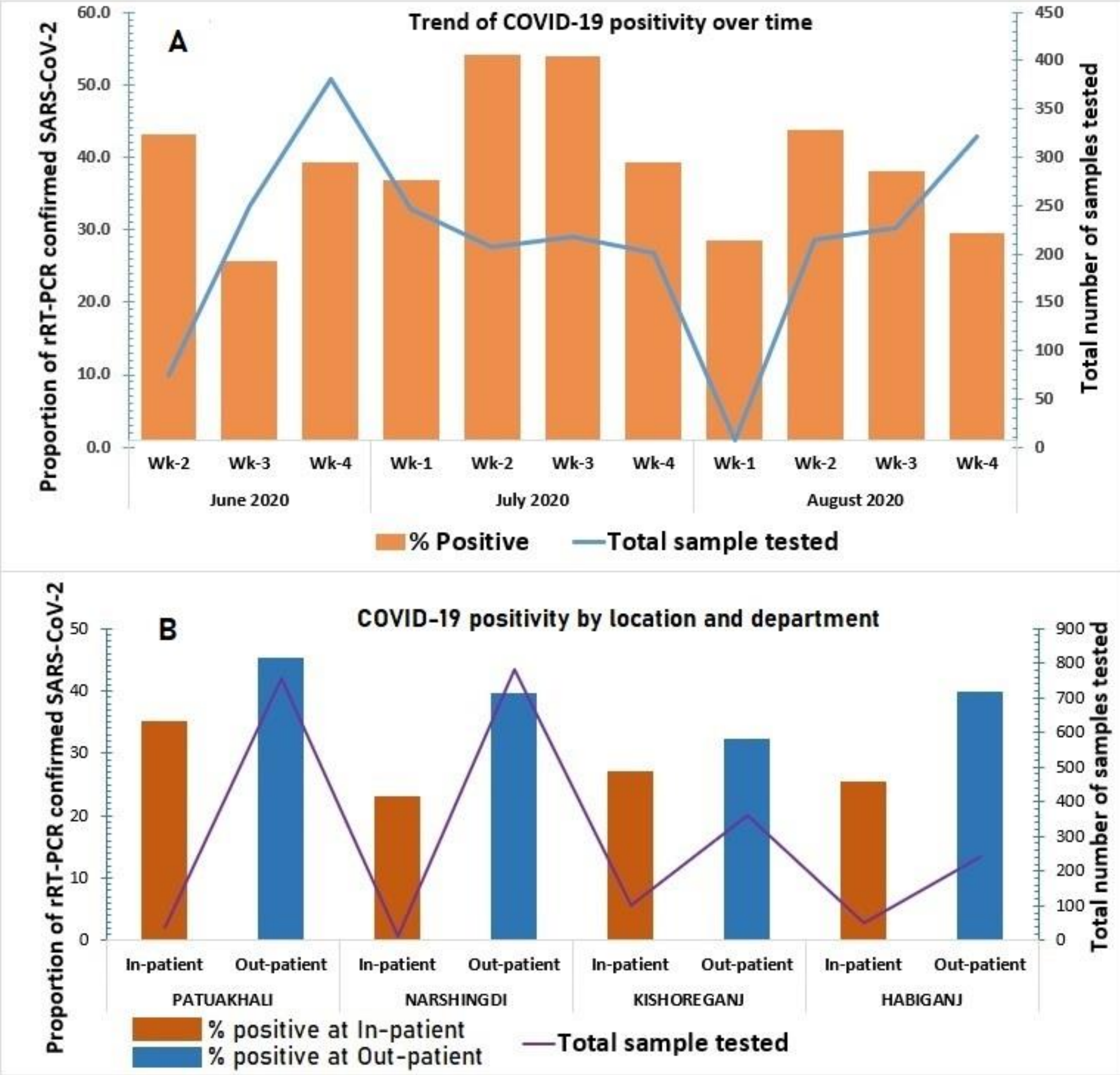
**Table 2.** Factors associated with adverse outcome (death) among COVID-19 positive patients in selected hospitals of Bangladesh, June-August 2020.

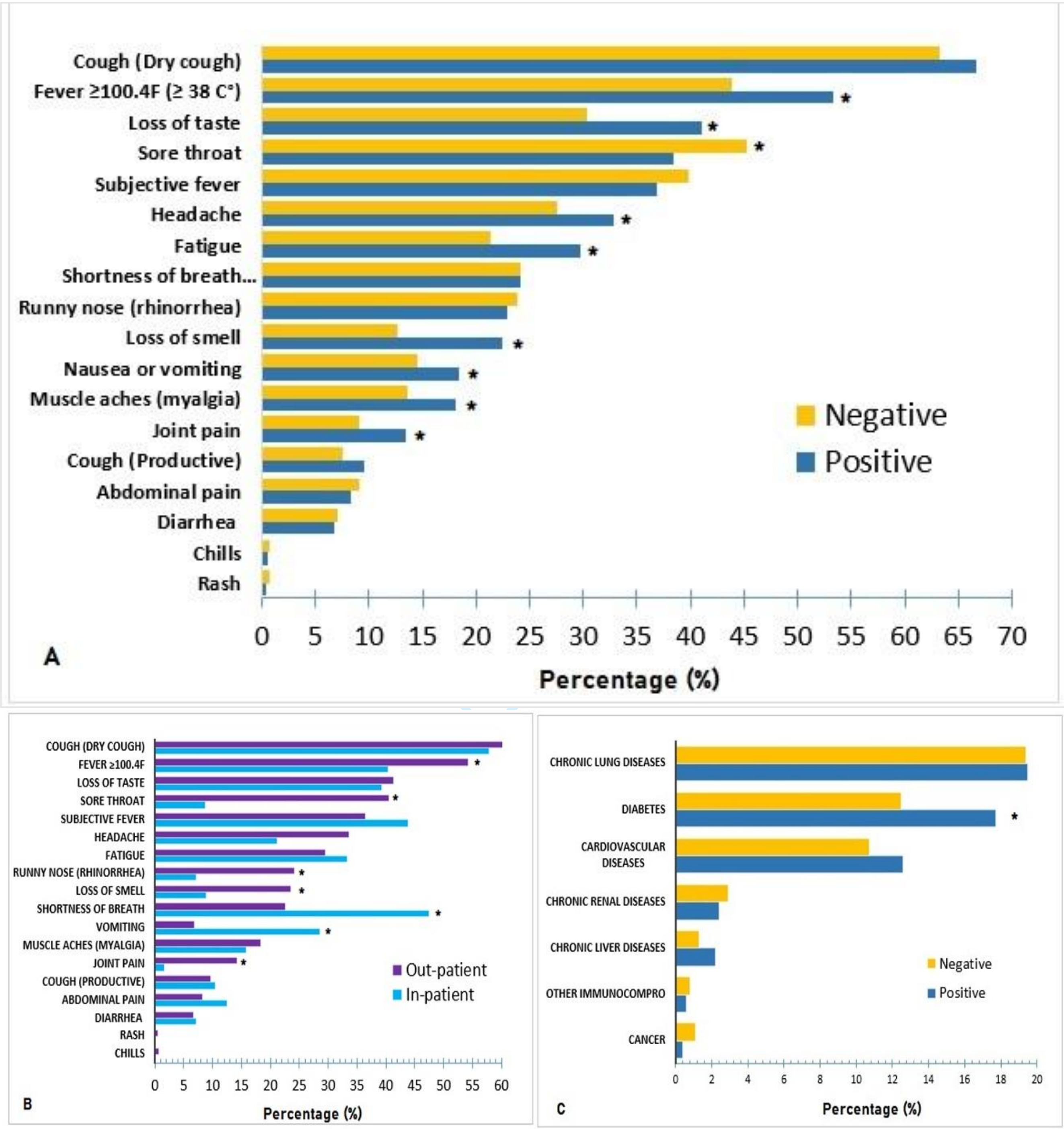
| Factors | | Frequency N=922 | Death n=21 Frequency (%) | Odds ratio OR (95% CI) | Adjusted odds ratio AOR (95% CI) |
|---|---|---|---|---|---|
| Age* | 0-59 years | 812 | 8 (1%) | 1 | 1 |
| | ≥ 60 years | 110 | 13 (11.8%) | 13.5 (5.4-33.3) | 13.9 (5.5-34.5) |
| Sex | Male | 654 | 14 (2.1%) | 1 | 1 |
| | Female | 268 | 7 (2.6%) | 1.2 (0.5-3.0) | 1.5 (0.55-4.0) |
| Health care worker | Yes | 83 | 0 (0%) | 1 | 1 |
| | No | 839 | 21 (2.5%) | - | - |
| Symptoms | ≤3 symptoms | 314 | 7 (2.2%) | 1 | 1 |
| | >3 symptoms | 608 | 14 (2.3%) | 1.0 (0.4-2.5) | 1.4 (0.52-3.9) |
| Shortness of breath* | No | 700 | 4 (0.6%) | 1 | 1 |
| | Yes | 222 | 17 (7.7%) | 14.4 (4.8-43) | 9.7 (3.0-30.4) |
| Comorbidity* | No | 538 | 2 (0.4%) | 1 | 1 |
| | Yes | 384 | 19 (4.9%) | 13.9 (3.2-60) | 4.8 (1.05-21.7) |
| History of smoking | No | 812 | 14 (1.7%) | 1 | 1 |
| | Yes | 110 | 7 (6.4%) | 3.9 (1.5-9.8) | 2.2 (0.71-7.1) |
| Treatment received* | OPD | 865 | 12 (1.4%) | 1 | 1 |
| | inpatient | 57 | 9 (15.8%) | 13.3 (5.3-33) | 3.4 (1.2-9.8) |

| | | | | | |
|---|---|---|---|---|---|
| Duration of hospital attendance from the onset of symptom* | ≥ 2 days | 880 | 17 (1.9%) | 1 | 1 |
| | < 2 days | 42 | 4 (9.8%) | 5.4 (1.8-17.1) | 4.7 (1.2-17.8) |

***Factors with a significant difference between groups***


COVID-19
Positive
Negative
N
INDIA
Kishoreganj
31%
Habiganj
37%
INDIA
39%
Narshingdi
INDIA
45%
Patuakhali
BAY OF BENGAL
80 km
40 mi


A
Trend of COVID-19 positivity over time
Proportion of rRT-PCR confirmed SARS-CoV-2
Total number of samples tested
60.0
50.0
40.0
30.0
20.0
10.0
0.0
450
400
350
300
250
200
150
100
50
0
Wk-2 Wk-3 Wk-4 Wk-1 Wk-2 Wk-3 Wk-4 Wk-1 Wk-2 Wk-3 Wk-4
June 2020
July 2020
August 2020
% Positive
Total sample tested
B
COVID-19 positivity by location and department
50
40
30
20
10
0
900
800
700
600
500
400
300
200
100
0
In-patient Out-patient In-patient Out-patient In-patient Out-patient In-patient Out-patient
PATUAKHALI
NARSHINGDI
KISHOREGANJ
HABIGANJ
% positive at In-patient
% positive at Out-patient
Total sample tested


Cough (Dry cough)
Fever ≥100.4F (≥ 38 C°)
Loss of taste
Sore throat
Subjective fever
Headache
Fatigue
Shortness of breath...
Runny nose (rhinorrhea)
Loss of smell
Nausea or vomiting
Muscle aches (myalgia)
Joint pain
Cough (Productive)
Abdominal pain
Diarrhea
Chills
Rash
Negative
Positive
0 5 10 15 20 25 30 35 40 45 50 55 60 65 70
A
Percentage (%)
COUGH (DRY COUGH)
FEVER ≥100.4F
LOSS OF TASTE
SORE THROAT
SUBJECTIVE FEVER
HEADACHE
FATIGUE
RUNNY NOSE (RHINORRHEA)
LOSS OF SMELL
SHORTNESS OF BREATH
VOMITING
MUSCLE ACHES (MYALGIA)
JOINT PAIN
COUGH (PRODUCTIVE)
ABDOMINAL PAIN
DIARRHEA
RASH
CHILLS
Out-patient
In-patient
0 5 10 15 20 25 30 35 40 45 50 55 60
B
Percentage (%)
CHRONIC LUNG DISEASES
DIABETES
CARDIOVASCULAR DISEASES
CHRONIC RENAL DISEASES
CHRONIC LIVER DISEASES
OTHER IMMUNOCOMPRO
CANCER
Negative
Positive
0 2 4 6 8 10 12 14 16 18 20
C
Percentage (%)

**Supplementary table 1**. Distribution of deaths among COVID-19 positive patients in selected hospitals of Bangladesh, June-August 2020.

| | **Hospital death n= 16** | | **Home death n=5** | |
|---|---|---|---|---|
| **Age (years)** | | | | |
| Lowest, highest | 40, 85 | | 51, 90 | |
| Median (IQR) | 65 (55-69) | | 64 (52-70) | |
| **Sex** | | | | |
| Male | 11 (69) | | 3 (60) | |
| **Timing of death from symptom onset** | | | | |
| 0-7 days | 6 (38) | 6 (38) Cum. | 3 (60) | 3 (60) Cum. |
| 8-15 days | 9 (56) | 15 (94) | 2 (40) | 5 (100) |
| 16-40 days | 1 (6) | 16 (100) | | |
| **Manner of death** | | | | |
| Disease | 16 | | 5 (100) | |
| Accident | 0 | | 0 | |
| Sudden death (heart attack) | 0 | | 0 | |
| **Comorbidity present (anyone)** | 15 (94%) | | 4 (80) | |
| DM | 9 (56) | | 2 (40) | |
| Asthma/COPD | 4 (25) | | 2 (40) | |
| Heart disease/HTN | 6 (37) | | 2 (40) | |
| Chronic renal disease | 4 (25) | | 0 | |
| Cancer (uterine) | 1 (6) | | 0 | |
| **Clinical course of treatment** | | | | |
| Oxygen required | 16 (100) | | 3 (60) [ 2 got oxygen at home] | |
| ICU admitted | 3 (19) | | | |
| CCU admitted | 1 (6) | | | |
| Dialysis required | 1 (6) | | | |
| **Cause of death as stated from hospital as reported** | | | | |
| COVID-19 + Respiratory failure | 14 (88) | | | |
| Pneumonia | 1 (6) | | | |
| Chronic renal failure | 1 (6) | | | |

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

| | Item No | Recommendation | Page No |
|---|---|---|---|
| **Title and abstract** | 1 | (*a*) Indicate the study's design with a commonly used term in the title or the abstract | 1 |
| | | (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found | 1 |
| **Introduction** | | | |
| Background/rationale | 2 | Explain the scientific background and rationale for the investigation being reported | 4-5 |
| Objectives | 3 | State specific objectives, including any prespecified hypotheses | 5 |
| **Methods** | | | |
| Study design | 4 | Present key elements of study design early in the paper | 6 |
| Setting | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | 6-7 |
| Participants | 6 | (*a*) Give the eligibility criteria, and the sources and methods of selection of participants | 6 |
| Variables | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable | 8 |
| Data sources/ measurement | 8* | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group | *NA* |
| Bias | 9 | Describe any efforts to address potential sources of bias | NA |
| Study size | 10 | Explain how the study size was arrived at | NA |
| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why | 7 |
| Statistical methods | 12 | (*a*) Describe all statistical methods, including those used to control for confounding | 7 |
| | | (*b*) Describe any methods used to examine subgroups and interactions | 7 |
| | | (*c*) Explain how missing data were addressed | NA |
| | | (*d*) If applicable, describe analytical methods taking account of sampling strategy | |
| | | (*e*) Describe any sensitivity analyses | |
| **Results** | | | |
| Participants | 13* | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed | 8 |
| | | (b) Give reasons for non-participation at each stage | NA |
| | | (c) Consider use of a flow diagram | NA |
| Descriptive data | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders | 8-9 |
| | | (b) Indicate number of participants with missing data for each variable of interest | NA |
| Outcome data | 15* | Report numbers of outcome events or summary measures | 7-10 |
| Main results | 16 | (*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included | 10 |

| | | | |
|---|---|---|---|
| | | (*b*) Report category boundaries when continuous variables were categorized | NA |
| | | (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period | |
| Other analyses | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses | NA |
| **Discussion** | | | |
| Key results | 18 | Summarise key results with reference to study objectives | 10-15 |
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias | 15 |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence | 16 |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results | 15 |
| **Other information** | | | |
| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based | 16 |

*Give information separately for exposed and unexposed groups.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.