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Technical Report 16

Epidemiology and clinical manifestations of COVID-19 during the early outbreak period based on reports from 10 countries

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Highlights

- Presentation of fever varied between 50-100% of cases at presentation.

- Some of the patients with COVID-19 were asymptomatic at diagnosis.

- Lack of local data on clinical presentation and management was a major limitation at the time of the survey.

Background

China has reported a cluster of cases of pneumonia in people linked with the Huanan Seafood Wholesale Market in Wuhan, Hubei Province since 8 December 2019. On 9 January 2020, Chinese health authorities confirmed that the cause of this viral pneumonia outbreak was a novel coronavirus, 2019-nCoV. This novel virus spread across Wuhan, which is a large city located in Central China of more than 11 million people (1). The number of identified cases has been steadily growing over the following months from China and also from several other countries. COVID-19 has now been declared as a Public Health Emergency of International Concern by the World Health Organization (WHO). Given the spread of the novel coronavirus and its impact on human health, the research community has responded rapidly with

many preliminary articles already published. We have conducted a review to summarize the findings of these, with an aim to provide evidence on the epidemiology and clinical features of confirmed COVID-19 cases.

Compilation of the evidence

Literature for the review was identified by searching online databases such as Google Scholar and PubMed. Scientific publications in peer-reviewed journals from 10 countries as case reports/case series/descriptive studies or comparative studies on confirmed COVID-19 patients were included in the review. Data pertaining to the sociodemographic details, typical and atypical symptoms at presentation, past medical history, clinical course of disease were extracted.

Studies included in the review consisted of COVID-19 patients diagnosed by reverse transcription polymerase chain reaction (RT-PCR) except one study from China, which had compared 19 patients with COVID-19 positive pneumonia with 19 pneumonia patients who were negative for COVID-19 (2). One study from China reported 113 deceased patients confirmed with COVID-19 in Wuhan (3). Several other countries described the first cases reported from their country (4-9).

● Age and sex distribution

The age of patients varied from six months to ≥ 85 years. The majority belonged to the 40-50-year age group. In almost all studies, except for the individual case reports, the affected were mostly males.

● Clinical manifestation

COVID-19 confirmed patients had shown a wide spectrum of clinical manifestations ranging from mild to severe, with some leading to fatal complications.

The most commonly reported symptoms are fever, cough, fatigue or myalgia, sore throat (1-4, 10-17, 18), whereas less commonly reported symptoms were headache, diarrhoea, productive cough and

runny nose (3, 11-12, 15). Symptoms at presentation and during the course of the illness of confirmed cases are summarised below.

- Fever was present in 50-100% of the cases at presentation.

  There were two case reports from Singapore and Germany, where the cases were asymptomatic at presentation (5, 19).

  One study from China, which extracted data from 1099 patients reported fever in 43.8% on admission and 88.7% during hospitalization (1). Chills were reported in four studies (7, 18-20).According to one study in China, fever and cough were the dominant symptoms while gastrointestinal symptoms were uncommon, suggesting a difference in the viral tropism compared to SARS-CoV, MERS-CoV and seasonal influenza.

  The absence of fever in COVID-19 was more frequent than in SARS-CoV (1%) and MERS-CoV infection (2%). This highlights that afebrile patients could be missed if the surveillance case definition focuses on fever detection (1).

- The presentation of cough varied between 47-81% (1-6, 8, 12, 14-15, 18, 21-22). Several studies specified it as a dry cough (6-7, 10, 12, 15) while a few reported it as an expectoration (13, 21).

- General malaise/myalgia was reported in five studies (3, 10, 18-19, 23), whereas fatigue was reported in three studies (2-4). One study reported that 50% had fatigue at presentation (3).

- Sore throat was reported in six studies and the percentage varied from 5% to 61%. (2, 3, 5, 10, 23). According to the case report from Germany, sore throat was present at the onset of symptoms but not at the stage of presentation to disease diagnosis (19).

- Shortness of breath was reported in six studies (3-5, 13, 15, 18). A Chinese study which reported data of 62 patients with mild disease, shortness of

breath was present only in 3% on admission (13). In three other studies, it was present in nearly 31% of the cases (3-4, 15). It was noted that at the time of presentation, shortness of breath had been reported in 62% (n=70) among those who died (n=113) and in 31%, (n=50) among those who recovered (n=161) (4).

- Rhinorrhoea or runny nose was reported in three studies and the percentage was less than 10% (3, 5, 7).

- Diarrhoea was reported in six studies and this percentage varied between 2-28% (3-5, 12-13, 15).

- Chest tightness was reported in three studies from China with a percentage varying from 2-38%. (2-4). It was noted that in one study, chest tightness was more commonly reported among those who eventually died (49%) than those who recovered (30%) (4).

- Headache, dizziness and even confusion had been reported in few studies (3-4, 12).

Clinical course and outcome

- According to a summary report of 72,314 cases from China, most cases were classified as mild (81% with no pneumonia or mild pneumonia), whereas 14% had severe (dyspnoea, blood oxygen saturation< 93%, lung infiltrates> 50%) and 5% were critical (respiratory failure, septic shock and multi organ failure) (24). The overall case fatality rate (CFR) was reported as 2.3%, however cases in those aged 70-79 years and 80 years and above were reported as 8.0% and 14.8%, respectively. No deaths were reported among mild and severe cases. The CFR was 49% among the critical cases and also increased with pre-existing comorbidities such as cardiovascular disease (10.5%), diabetes (7.3%) and chronic respiratory disease (6.3%) (24).

- The median (IQR) duration of days from onset of symptoms to hospital admission was 4.0 (1.0-7.0) for those who recovered (1) and 10.0 (7.0-13.0) for those who succumbed to COVID-19 (4).

- The median (IQR) duration of days from the onset of symptoms to outcome was reported from 12.0 (95% CI=6.0-17.0) to 22.0 (95% CI=16.8, 27.3) (1-4 ,8, 12).

- Those who required ICU care during the course of illness varied between 5-23%. The median (IQR) duration from the onset of symptoms to ICU admission was 9.5 (95% CI=7.0, 12.0) days (2-4).

Gaps in existing knowledge

The data had been collected mostly from available hospital records and in some studies the incomplete data had been collected referring to the treating healthcare workers, which could have included a recall bias. (1,4). Further, many patients were still at hospital, at the time of data extraction and as a result, some data would have been censored. They may have missed mild or asymptomatic patients who were not hospitalized. Further, the data were clinically driven and not systematic. The Sri Lankan studies or even South Asian studies related to clinical presentation of COVID-19 patients were rather scarce.

Public health implications

COVID-19 is a novel coronavirus, which emerged from China in December 2019 and which has spread to over 200 countries within four months, causing a massive pandemic. Since this is a new disease, knowledge is evolving day by day. Studying epidemiology and clinical presentation are key factors in identifying a disease. This would invariably help the epidemiologists in identifying the cases early, which would limit the spread in the community. Studying the course of the illness may help in deciding the treatment/management options, e.g. Can the mild/asymptomatic cases be observed in a separate centre or at even at home not burdening the main treatment centre? Lessons learnt from the countries that are successfully managing the disease

can be adopted after considering the individual country context.

Application of evidence to Sri Lanka

Most of the studies have collected data using standardized reporting formats such as International Severe Acute Respiratory and Emerging Infection Consortium case report forms. Using a common format and uploading the data at a common forum may increase the comparability of data, making it accessible to many stakeholders and preventing duplication of work.

In applying evidence to Sri Lanka, lack of data on clinical presentations is a major limitation for comparison. Thus, collecting and sharing data related to patient presentations, clinical course of the illness, treatment options etc. is common, yet a locally adaptive format, it would increase the usefulness of the data is a timely need. If the data can be entered to. Initially, the data obtained from the patients who were already discharged from hospital, would be helpful in decision making related to management options. It is recommended that the data be shared with relevant stakeholders (e.g. clinicians, public health experts, statisticians, etc.) whilst maintaining the ethical and administrative considerations.

Author Declaration

Author contributions: NP coordinated the data compilation and drafted the manuscript. SP, SJ, SAH and NDW were involved in conceptualization of the study and final editing of the manuscript. NP, NF, CW, SN, HJ, SD, MF, CR, TS, NL and SW were involved in data compilation.

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