Evidence note

The clinical spectrum of COVID-19

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Ministry of Health and Population
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Background

As a part of sharing evidence to support the health sector response to COVID-19 pandemic, the Ministry of Health and Population (MoHP) through the knowledge café secretariat at the Policy, Planning and Monitoring Division (PPMD) organised a virtual Knowledge Café (a platform for promoting the use of evidence) on clinical spectrum of CVOID-19 on 12 May 2020. The meeting was attended by senior Government officials, health external development partners and other stakeholders, and national and international clinicians who provided their inputs based on the latest evidence as well as their first-hand experiences in treating COVID-19 patients. This evidence note is a product of the knowledge café discussion and presentation, with a rapid evidence synthesis.

Clinical Spectrum of disease

Results illustrated in table 1 and 2 present the clinical spectrum of disease in general population and in paediatric population, respectively. In general, 81% of the COVID-19 cases can have mild (and moderate) symptoms while other 14% can have severe and remaining 5% can have critical disease in general population. (Wu & McGoogan, 2020)

In paediatric population, 4.4% were asymptomatic, 50.9% had mild, 38.3% had moderate, 5.2% had severe disease. Only 0.6% were found to develop critical disease (Dong et al., 2020).

Table 1: Clinical spectrum of disease (Wu & McGoogan, 2020)

Spectrum	Clinical Presentation	%
Mild (and moderate)	Mild symptoms up to mild pneumonia	81
Severe:	Dyspnoea, hypoxia, or >50% lung involvement on imaging	14
Critical	Respiratory failure, shock, or multiorgan system dysfunction	5

Table 2: Clinical spectrum in paediatric population (Dong et al., 2020)

Spectrum	Clinical Presentation	%
Asymptomatic	No clinical s/s; normal chest imaging	4.4
Mild	Constitutional symptoms, upper respiratory infection and mild GI symptoms	50.9
Moderate	Pneumonia with fever and cough but no obvious hypoxemia Subclinical lung lesions in chest CT.	38.8
Severe	Progresses in around 1 week, and dyspnoea occurs, with central cyanosis, SpO2 < 92% with other hypoxia manifestations	5.2
Critical	Acute respiratory distress syndrome (ARDS) and multiple organ failure	0.6

Comorbidities

Results are of pooled prevalence for COVID-19 infected patients from a systematic review and meta-analysis (included 19 studies). With the total of 36.8% cases comorbidities, hypertension (18.6%), cardiovascular disease (14.4%,), diabetes (11.9%), chronic liver disease (3%), malignancies (2.5%) and COPD (1.8%) were the most prominent [Table 3].

Table 2: Comorbid conditions among COVID-19 patients (Rodriguez-Morales et al., 2020)

Conditions	%
Comorbidities	36.8
Hypertension	18.6
Cardiovascular disease	14.4
Diabetes	11.9
COPD	1.8
Malignancies	2.5
Chronic liver diseases	3

Table 4: Spectrum of diseases according to age group (Flaxman et al., 2020)

Age group	% of symptomatic cases requiring hospitalization	% of hospitalized requiring critical care	Infection fatality rate
0-9 years	0.1	5.0	0.002
10-19 years	0.3	5.0	0.006
20-29 years	1.2	5.0	0.030
30-39 years	3.2	5.0	0.080
40-49 years	4.9	6.3	0.150
50-59 years	10.2	12.2	0.600
60-69 years	16.6	27.4	2.200
70-79 years	24.3	43.2	5.100
80+ years	27.5	70.9	9.300

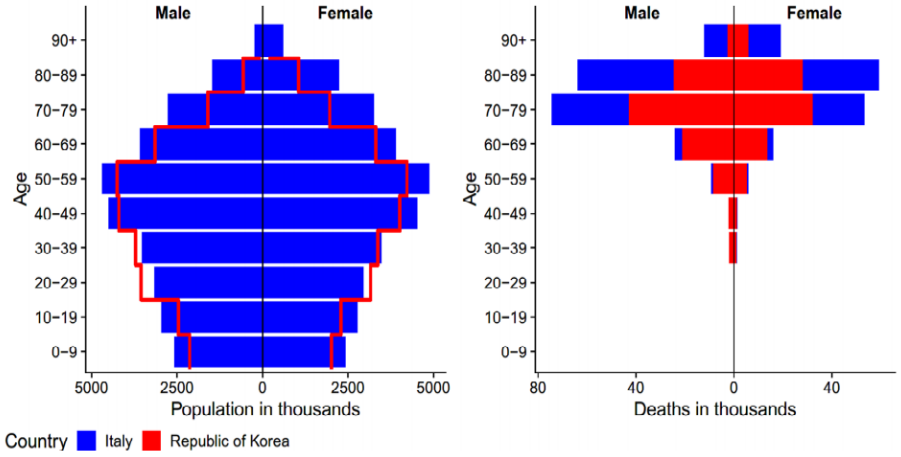

Figure 1: Population pyramid and death rates due to COVID-19 in Italy and South Korea (Dowd et al., 2020)

COVID-19 fatality was higher in elderly and increased with increasing age as shown in Table 4. Authors classed spectrum of disease according to the age group wherein percentage of symptomatic cases requiring hospitalization, critical care and fatality rate all increased with increasing age; 80 years and above being the most affected. (Flaxman et al., 2020)

Pyramids in Figure 1 illustrate how population age structure interacts with high COVID-19 mortality rates at older ages. Italy with higher proportion of elderly population has the larger number of fatalities due to COVID-19. (Dowd et al., 2020)

Clinical features, laboratory, and radiological findings

Fever was reported in almost nine out of ten infected individuals (88.7%). Fever seem to be more common in adults than in children (92.8% in adults vs 43.9% in children). Cough was next most common symptom presented by 57.6% of the cases. Like fever, cough was presented by almost half of the paediatric patients compared to adults (63% in adult vs 22% in adults). Among other clinical manifestations were dyspnoea (45.6%), myalgia (29.4%), sputum production (28.5%), sore throat (11%), headache (8%) and diarrhoea (6.1%) (Rodriguez-Morales et al., 2020) [Table 5].

Table 5: Clinical manifestations (Rodriguez-Morales et al., 2020)

Clinical Manifestation	%
Fever	88.7
Adult	92.8
Children	43.9
Cough	57.6
Adult	63.4
Children	22
Dyspnoea	45.6
Myalgia	29.4
Sputum production	28.5
Sore throat	11
Headache	8
Diarrhoea	6.1

Laboratory and radiological tests show that patients infected with COVID-19 were found with decreased albumin (75.8%), high C-reactive protein (58.3%), high in lactate dehydrogenase (LDH) (57.0%), lymphopenia (43.1%), and increased level of erythrocyte sedimentation rate (ESR) (41.8%). In chest X-rays, the pneumonia was

predominantly noted bilateral (72.9%); 7% higher in children compared to adults with image findings of ground-glass opacity in 68.5%, in X-rays (Rodriguez-Morales et al., 2020)

Time of onset and duration of clinical presentation

The median duration of fever was 12 days and the cough persisted for 19 days among survivors. Complications such as ARDS, sepsis and septic shock, acute cardiac injury, acute kidney injury and secondary infection developed at a median of 12 days, 9 days, 15 days, 15 days and 17 days. The median duration of viral shedding was 20 days from illness onset in survivors vs. non-survivors who continued shedding virus till death (Sharma et al., 2020).

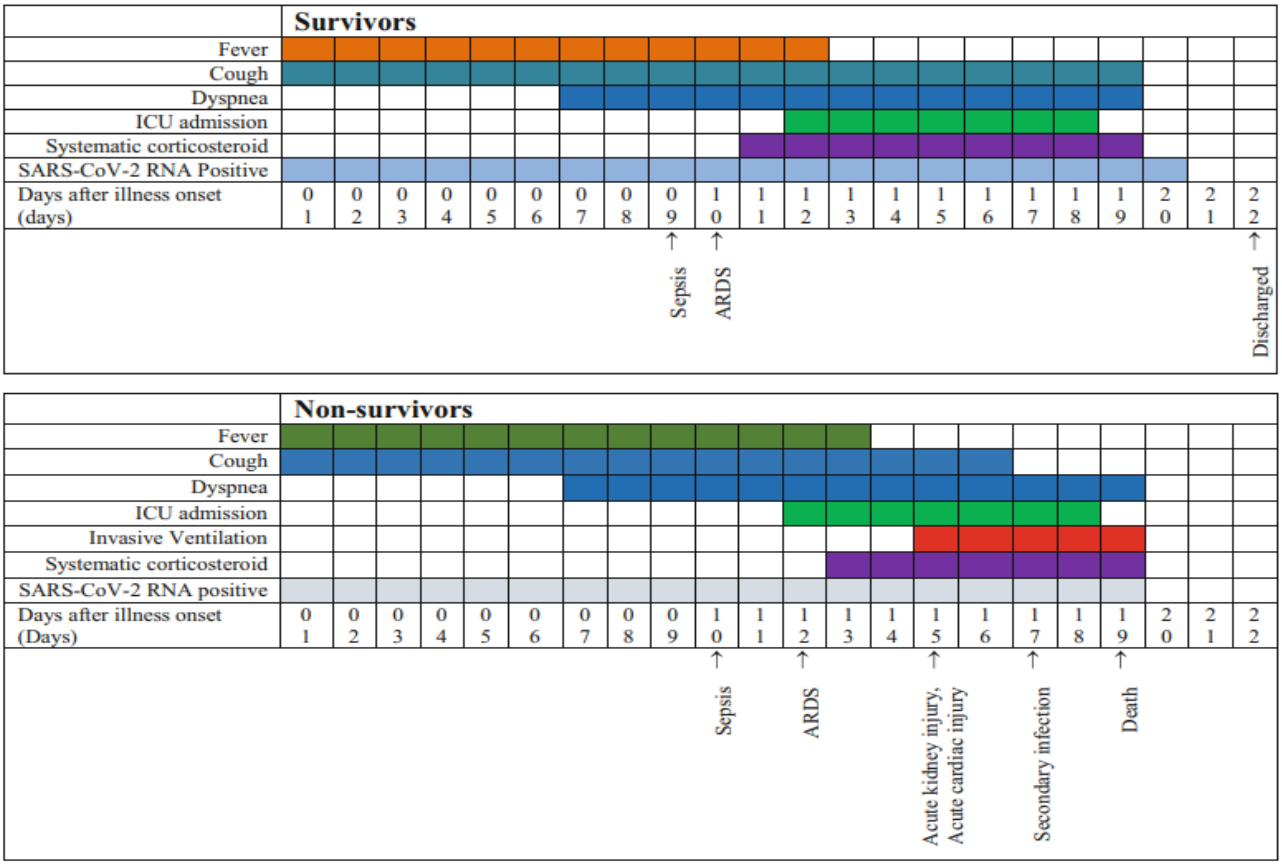

Figure 2: Course of illness among COVID-19 survivors and non survivors (Sharma et al., 2020)

Clinical management of the COVID-19 cases

Mild to moderate cases can be managed as suggested below (Centers for Disease Control and Prevention [CDC], 2020):

- Patients with a mild clinical presentation (absence of viral pneumonia and hypoxia) may not initially require hospitalization, and many patients will be able to manage their illness at home.
- The decision to monitor a patient in the inpatient or outpatient setting should be made on a case-by-case basis.
- This decision will depend on the clinical presentation, requirement for supportive care, potential risk factors for severe disease, and the ability of the patient to self-isolate at home.
- Patients with risk factors for severe illness should be monitored closely given the possible risk of progression to severe illness in the second week after symptom onset.

Inpatient management of severe cases involves supportive management of following conditions (CDC, 2020):

- Pneumonia,
- Hypoxemic respiratory failure/Acute respiratory distress syndrome (ARDS),
- Sepsis and septic shock,
- Cardiomyopathy and arrhythmia,
- Acute kidney injury, and
- Complications from prolonged hospitalization including secondary bacterial infections,
- Thromboembolism,

- Gastrointestinal bleeding, and
- Critical illness polyneuropathy/myopathy

Complications

Varying complications were seen of which the most significant RNAemia (detection of viral RNA in the blood). This was reported in 96.8% of the patients. Second, ARDS was seen among 32.8% of infected patients. Acute cardiac injury (13%), acute kidney injury (7.9%), shock (6.2%) and secondary infection (5.6%) were among other complications related to COVID-19. Furthermore, 87.9% infected patients were reportedly hospitalized (Rodriguez-Morales et al., 2020).

Table 6: Complications due to COVID-19(Rodriguez-Morales et al., 2020)

Complications	Percentage
RNAemia	96.8
Adult	96.6
Children	98.3
ARDS	32.8
Acute Cardiac injury	13
Acute Kidney injury	7.9
Shock	6.2
Secondary infection	5.6
Hospitalization	87.9

Can BCG vaccine prevent disease or reduce mortality?

A study by Hegarty et al. (2020) that compared incidence of COVID-19 in 178 countries with and without current national programme on BCG vaccination and revealed that incidence and mortality can be lower in countries with BCG vaccination. The incidence rate was 38.4 per million in countries with BCG vaccination and 358.4 per million in countries without BCG vaccination. The death rate was 4.28 per million in countries with BCG vaccination while it was 40 per million without BCG vaccination. However, findings on protective effect of BCG vaccination are contradictory. Time adjusted analysis by Bodova et al (2020) did not find any associations with case fatality rates (CFR), and suggested that the noted differences in CFR estimates are at present are probably because of differences in testing and case reporting between countries. The findings by Hegarty et al (2020) are further validated by another study Hansel et al. (2020) which found that when analysis is confined to countries with high testing rates, there was no longer significant association between number of COVID-19 cases per million population with and without BCG vaccination. In a scientific brief on 12th April, World Health Organization (2020) states there is no evidence that BCG protects people from COVID-19 and that ecological studies that compared the BCG vaccination and COVID-19 cases across countries are prone to significant bias from many confounders, including differences in national demographics, testing rates for COVID-19 virus infections, and the stage of the pandemic in each country .

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