COVID-19 Pandemic Management of LMICs

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The World Bank has historically classified countries according to their per capita gross national income (GNI) into three groups: high-income countries (or HICs), middle-income countries (or MICs), and low-income countries (or LICs). In 2020, LICs were 32, suffering high rates of illnesses and infections due to the lack of clean water, low sanitation levels, malnutrition, and the lack of access to quality medical care. Approximately 5 billion people lived in MICs, representing over 70% of the world population. There are a total of 105 MICs. Only 77 countries were classified by the World Bank as HICs. The management of the COVID-19 pandemic represents a challenging process, especially for low- and middle-income countries (LMICs) due to the serious economic and health resource problems it generates.

COVID-19 | low-and middle-income countries (LMICs) | infection prevention | triage

1. Infection Prevention and Control

In LMICs, a focused testing on selected patients instead of a random screening would be less stressful for the healthcare system [1]. COVID-19 tests should target patients with coexisting diseases or atypical presentations, pregnant women, and health workers. For other patients, a clinical case definition based on symptoms and radiology results should be adopted, such as that proposed by the Haitian Ministry of Public Health and Population [2].

Other problems are the lack of a country-based testing plan, the lack of sufficiently trained staff for performing RT-PCR, and insufficient supplies of the reagents and kits for nucleic acid extraction and molecular detection, needed to perform a high number of tests for SARS-CoV-2 [3]. Rapid test kits are an option to allow LMICs to perform diagnostic tests faster [1].

In 2009, the World Health Organization Regional Office for Africa (WHO AFRO) launched the Stepwise Laboratory Quality Improvement Process Towards Accreditation (SLIPTA) program with the aim to strengthen laboratories' compliance with international standards through training and mentoring [4]. Nevertheless, the mode of testing for COVID-19 in Africa is through reference laboratories and central laboratory testing. Sub-Saharan Africa (SSA) countries can take advantage of GeneXpert®, a multi-disease diagnostic platform used initially to test tuberculosis (TB) and later adapted for human immunodeficiency virus (HIV) and Ebola [5]. The GeneXpert® is a molecular testing platform which can be located in all laboratories for immediate diagnostics [6]. It processes samples onsite, reducing transportation time and test waiting times to only 45 min. It has been successfully used in Madagascar, showing that the use of the GeneXpert® platform to screen patients with SARS-CoV-2 in LMICs is relevant and achievable and should be adopted in countries with difficult access to laboratories and an already pre-existing GeneXpert® network [7]. In order to slow down the spread of COVID-19, the WHO recommends infection control interventions to reduce the risk of transmission, in particular, avoiding close contact with people suffering from acute respiratory infections, frequent hand washing especially after direct contact with infected people or their environment, and avoiding unprotected contact with farm or wild animals [8]. Worldwide, governments have established regulations that require social distancing, the closure of non-essential businesses, travel restrictions and, in many cases, quarantine. Although these measures are necessary for public health, social restrictions are difficult to realize in LMICs due to money-related livelihood problems [9]. Furthermore, a complete commercial shutdown like those imposed in China, Europe, or the United States is not feasible when a day without work is tantamount to a day without food [2].

Appropriate personal protective equipment (PPE) is required by all available guidelines for the management of COVID-19 patients. PPE is in enormous demand around the world, and its procurement will thus prove especially difficult in LMICs [10]. Some low-cost suggestions were proposed for creating or extending PPE. In emergency situations, raincoats and windcheaters were used as gowns, while swimming caps, goggles, and transparent paper were used as PPE [11].

2. Triage

In resource-limited settings, it is necessary to adopt a simple and rapid logarithm to decide who requires isolation and targeted testing for SARS-CoV-2. The most recent recommendations suggest that initial screening to identify individuals with COVID-19 include signs and symptoms based on standard case definitions of COVID-19 disease [12]. In these countries, other endemic febrile illnesses are particularly common, and their presentation could easily be similar to that of COVID-19. Clinician should consider these diseases as part of the comprehensive clinical diagnostic process.

Being able to estimate which patients will develop severe disease would allow hospitals to better utilize already limited resources more effectively. In this way, hospitals could stop admitting patients at low risk of deterioration by avoiding unnecessary treatment. A severity score based on the COVID-19 disease definition should be performed for all suspected or confirmed COVID-19 cases before their access to the emergency department [12].

The approach should use the available technology. In LMICs, there are several problems regarding the availability of radiologic diagnostic modalities, the status of the machines, and the availability of clinical staff who are skilled in performing and interpreting the exams [12].

In Uganda, Ayebare et al. proposed an algorithm triage based on common COVID-19 symptoms, such as fever or cough. When these symptoms are found in combination with the epidemiological risk, patients are isolated by adopting appropriate measures for infection prevention and control, and the SARS-CoV-2 test is performed [13].

In India, Nayan et al. proposed triaging by medical history and symptom-based test probability assessment for COVID-19. Only eligible patients undergo further investigations. Due to the poor healthcare resources, this approach is fast, saves important resources, and decreases the risk of transmission of the infection to the health workers [14].

3. Infrastructure and Intensive Care Unit

In LMICs, laboratories are often located in the capital cities, so that early diagnosis and isolation becomes difficult [15]. Furthermore, the infrastructures for the screening and treatment of COVID-19 are not separate from the ones devoted to non-COVID-19 healthcare, facilitating the spread of the infection.

The number of hospital beds and health workers is generally lower compared to that in HICs [16]. The WHO reports only 0.8 hospital beds per 1000 people in LICs and 2.3 in MICs. On the other hand, HICs have 5.3 hospital beds per 1000 people [17]. According to the WHO, 90% of LICs have fewer than 10 medical doctors per 10,000 people, compared to only 5% of HICs. Up to 93% of LICs have fewer than 40 nursing personnel per 10,000 people, compared to only 19% of HICs [17].

Whenever published data are available, the number of ICU beds is insufficient with respect to the population of LMICs [18]. The most recent data available from the WHO indicate that Africa has fewer than 5000 ICU beds, corresponding to five beds per one million people. In Europe, by comparison, there are 4000 beds per one million people.

In other countries, heterogeneous regional distribution and payer-based access are major barriers for the equitable delivery of critical care, despite a sufficient number of ICU beds [19]. In Brazil, there are about 100 ICU beds for every million people, but their distribution is not uniform among the different regions: the states of São Paulo (~18,000 ICUs), Rio de Janeiro (~7000 ICUs), and Minas Gerais (~6000 ICUs) concentrate the ICUs, and most of them are located in the capital cities [20]. Furthermore, long distances and high transportation costs commonly result in delayed presentation of critically ill patients.

The ICU equipment is often old and poorly serviced. Mechanical ventilators tend to be old, and many hospitals do not have oxygen or medical gas to drive them [21][22]. Generally, equipment maintenance is poorly performed if available, and funding for capital development is limited. When funding is available, the procurement system is plagued by corruption, leading to a fraudulent assignment.

WHO developed a document providing recommendations, technical guidance, standards, and minimum requirements for setting up and operating Severe Acute Respiratory Infection (SARI) treatment centers in LMICs. Important guidance in setting up a SARI treatment center in LMICs is given in a practical manual by the WHO entitled “*Severe acute respiratory infections* *treatment centre: practical manual to set up and manage a SARI treatment centre and a SARI screening facility in health care facilities*” [23].

4. Treatment

To date, remdesivir is the only antiviral recommended for use in hospitalized patients with COVID-19 [24]. It was first described in the literature in 2016 as a potential treatment for Ebola [25]. Remdesivir has been studied in several clinical trials for the treatment of COVID-19. The Food and Drug Administration (FDA) granted an Emergency Use Authorization (EUA) on 1 May 2020 [26]. Remdesivir was subsequently granted full approval as a COVID-19 treatment on 22 October 2020 [27].

The HIV antiretroviral combination lopinavir/ritonavir has also been proposed as a treatment for COVID-19 [28]. Although it has in vitro activity against SARS-CoV, higher than tolerable levels of the drug might be required to achieve inhibition in vivo [29][30]. Lopinavir/ritonavir and the other HIV protease inhibitors are not recommended for the treatment of COVID-19 according to the COVID-19 Treatment Guidelines Panel [24].

Chloroquine, an older drug used as an antimalarial, and its derivative hydroxychloroquine have become popular in an effort to find an effective treatment for COVID-19. In vitro, hydroxychloroquine shows superior activity against COVID-19 compared with chloroquine [31]. Despite the initial excitement about the potential significant effectiveness of chloroquine and hydroxychloroquine for treating COVID-19, recent studies suggest little to no benefits in using these drugs for COVID-19 treatment. Nevertheless, they are still likely to be considered as a potential therapy by many in the fight against COVID-19, especially in LMICs [32].

Severe forms of COVID-19 can lead to a systemic inflammatory response with sequelae of lung injury and multisystem organ dysfunction. Corticosteroids can be considered a therapeutic option for critically ill patients. Dexamethasone is a low-cost corticosteroid and it has recently been shown to significantly reduce mortality in patients most severely affected by COVID-19 [33].

LMICs will need access to these treatments at minimal prices to ensure that all who need them can be treated. A recent report shows that COVID-19 treatment drugs could be produced at very low prices, from $1 to $29 per course [34]. Some of these drugs are already offered as generics at prices close to the production cost, in LMICs. The Global Fund for AIDS, Tuberculosis, and Malaria (GFATM) and the President’s Emergency Plan for AIDS Relief (PEPFAR) are organizations whose purpose is to provide mass treatment for HIV, tuberculosis, and malaria at prices close to production costs [35][36]. In the current context, this system allows LMICs to access drugs to treat COVID-19 at affordable prices while mitigating the impact of the pandemic on other health programs.

Oxygen therapy and ventilation are two main non-pharmacological interventions used for COVID-19 patients.

In 2015, the “*Lancet Commission on Global Surgery*” revealed that approximately 24% of hospitals in LMICs lack oxygen supply [37].

Supplemental oxygen can be provided using simple nose prongs or face masks. Other modalities require specific equipment, which can be expensive and difficult to acquire, especially in LMICs. In the current state of the pandemic, several alternatives for respiratory support in the shortage of official devices are proposed, such as cheap CPAP helmets obtained by adapting diving mask [38].

In resource-limited settings, the provision of quality mechanical ventilation is challenging for several reasons [39]. First, a small number of the ICU beds are equipped with mechanical ventilators. Second, equipment maintenance can be problematic due to the frequent need to reuse single-use components, poor access to consumables such as heat and moisture exchangers and suction catheters, poor access to spare ventilator parts like flow meters, unreliable oxygen supply, and inconsistent electricity. Third, highly skilled capabilities are needed for quality ICU care in order to provide an adequate ventilatory support in severe cases of COVID-19. This will require extended staff training, not always possible. Finally, in emergency situations, a single ventilator is used to assisted multiple patients. This leads to an unequal delivery of gas volumes and pressures to the individual patients, compromising the individualized ventilator settings needed for optimal care.

In the context of the high importance of oxygen therapy for patients with severe COVID-19, the WHO provides a useful guidance on the different oxygen sources, entitled "*Oxygen sources and distribution for COVID-19 treatment centres*" [40].

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