COVID

Perspective

COVID-19: Lessons from the Past to Inform the Future of Healthcare

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Abstract: The emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and its global spread have left an indelible mark, disrupting multiple aspects of human life. It is therefore crucial to retrospectively analyze the factors that have contributed more to the initial inefficiency of the global response, thus enhancing preparedness and proactively addressing the risk of similar events occurring in the future. Critical areas were identified based on our expertise. Relevant bibliographic references were subsequently gathered through an open search of scientific databases to substantiate the concepts discussed in this article. The key issues that hindered an effective response to coronavirus disease 2019 (COVID-19) are numerous and multifaceted, and some of these will be critically examined in this article, including delayed identification of the pathogen, inadequate public health preparedness, inadequate therapeutic management, and deficiencies in laboratory diagnostics. From this analysis, key areas for improvement emerge to ensure more efficient responses to future health crises, including (i) enhancing and strengthening health information systems, (ii) improving pandemic preparedness and response planning, (iii) developing a resilient healthcare workforce, (iv) increasing investment in research and development, (v) expanding the use of telemedicine and digital health, (vi) ensuring universal access to healthcare, and (vii) improving public health communication and trust.

Keywords: COVID-19; SARS-CoV-2; healthcare; pandemics; evidence-based practice

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1. Introduction

The emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and its worldwide spread have left a permanent mark, causing widespread derangement across multiple facets of human existence [1]. From its initial emergence to its far-reaching consequences, the damages inflicted by the pandemic are profound and complicated. Beyond the direct biological impact of the virus on several organs and tissues, healthcare systems were strained to their limits, encountering a shortage of many indispensable medical supplies, the overwhelming of healthcare facilities, and the exhaustion of frontline healthcare personnel [2–6]. The long-term health consequences of coronavirus disease 2019 (COVID-19), mostly represented by a peculiar post-viral syndrome called "long-COVID", further compound the harm wrought by the pandemic [7].

In this previously unpredictable scenario, however, COVID-19 has represented an unprecedented occasion of improvement for healthcare, society, and governments. After nearly five years since the first reported case of SARS-CoV-2 infection, over 7 million official deaths (even if this figure may be underestimated by a factor of 3 or 4, which would make COVID-19 the second most deadly pandemic over the past century after the Spanish flu in 1918–1920) [8], the world has now transitioned towards a so-called post-pandemic (endemic) phase. In this "new normal", characterized by an inevitable coexistence with the virus and the continuous emergence of new variants [9], we need to look back and analyze what went wrong, in order to be more prepared and proactive in the not-so-unpredictable case that a similar event will hit again in the future. To this end, several aspects need to be investigated and troubleshot, identifying possible solutions that would help us be more prepared to face a hypothetical next pandemic challenge.

2. What Really Went Wrong?

The key issues that hindered an effective response during the COVID-19 pandemic are numerous and multifaceted, and some of these will be critically examined in this article, including the delayed identification of the pathogen, inadequate public health preparedness, inadequate therapeutic management, and deficiencies in laboratory diagnostics. Critical areas were identified based on our expertise. Relevant bibliographic references were subsequently gathered through an open search of scientific databases to substantiate the concepts discussed in this article.

2.1. Delayed Identification of the Pathogen

There is still an open debate about the real origin of SARS-CoV-2. Several theories have been formulated, the most accredited of which is zoonotic spillover [10]. Specifically, it seems quite likely that SARS-CoV-2 originated from an ancestral bat coronavirus, which has been transmitted to humans through an intermediate host species, possibly the pangolin. Throughout the process of transmission from the bat to the human host, the virus has incorporated a series of mutations, especially located in the spike protein and within the receptor binding domain, which have increased the affinity to host receptors, namely, the angiotensin converting enzyme 2 (ACE2) [11]. Accidental laboratory release (i.e., the so-called laboratory-leak hypothesis) is a second option, encompassing the possibility of a "laboratory accident" that may have allowed the release of the virus, by either incidental exposure of laboratory employees or infected laboratory animals [12]. The last and certainly less credible conspiracy hypothesis involves cognizant genetic engineering, according to which SARS-CoV-2 may have been intentionally generated for malicious scopes (e.g., as a biological weapon) [13]. Overall, the results of the new genomic analyses provide compelling evidence of an infection in the animals, significantly diminishing the plausibility of alternative hypotheses [14–16].

Irrespective of its origin, what seems to now be rather clear is that the SARS-CoV-2 spread earlier than the submission to GenBank of the sequence of this new coronavirus by a virologist working at the Peking Union Medical College in Beijing, on 28 December 2019, and the publication of the complete viral sequence by another Chinese virologist at Fudan University in January 2020, both circumstances occurring after the first cases were diagnosed in Wuhan on 17 November 2019 [17]. There are several proofs in support of this theory. Van Dorp et al. performed a large genome analysis using a set of over 7600 genome assemblies for identifying the emergence of genomic diversity over time, concluding that the time to the most recent common ancestor was between 6 October 2019 and 11 December 2019 [18]. This evidence was confirmed by another phylogenetic analysis that allowed to estimate that the SARS-CoV-2 zoonotic spillover may have occurred between August and October 2019 [19]. A serological survey conducted in Italy showed that, in September 2020, up to 14% individual enrolled in a prospective lung cancer screening trial tested positive for anti-SARS-CoV-2 antibodies [20]. In keeping with these findings, data derived from the UK-based Winter Coronavirus Infection Study, including around 28,000 subjects, showed that around 1% of the England population was already testing positive for SARS-CoV-2 in the middle of November 2019 [21]. However, Chinese officials reported to the World Health Organization (WHO) that they have finally identified the virus only on 9 January 2020, and the WHO published on Twitter the genetic sequences of an undetermined coronavirus received from China, making the information publicly available shortly afterwards [22].

It is now unquestionable that cases of "atypical pneumonia" started to increase as early as November 2019 in China, while a first case of SARS-CoV-2 infection was retrospectively diagnosed with molecular biology techniques at the end of November 2019 in Italy [22]. Thus, if we take for granted that SARS-CoV-2, or an ancestral form of this coronavirus, were already circulating across the world in August–September 2019, and caused the first severe forms of COVID-19 in November 2019, it can be estimated that 1 to 3 months may have been actually lost before officially recognizing the hazard. This late recognition of the threat has certainly contributed to diagnostic and treatment delays that have characterized the first wave of this pandemic. Although there is no definitive answer to the question of how many lives could have been saved if diagnostic tools had been available earlier to enable the timely isolation of positive cases and containment of outbreaks, it is reasonable to hypothesize that the number would have been substantially lower [23]. Regardless of the decision of the WHO regarding further inspections on this matter, it is imperative that all countries extend their full cooperation.

2.2. Inadequate Public Health Preparedness

Even before the pandemic, the financial crisis that occurred at the dawn of the new millennium has generated enormous threats to the vast majority of healthcare systems worldwide [24]. A scoping review published by Doetsch et al. highlighted that austerity policies have generated substantial limitation to healthcare access, mainly involving unmet needs, affordability, appropriateness, availability, and accommodation [25]. During the last (also called "great") recession period before the COVID-19 pandemic (i.e., between 2007–2009), cuts to healthcare financing had far-reaching consequences, mostly affecting the more vulnerable segments of the populations such as older patients, those bearing chronic conditions, and unemployed or economically inactive persons, along with individuals with lower socioeconomic status [25,26].

The continuous strain on healthcare resources persisted over subsequent years, and, even before the pandemic, many countries were already experiencing a decline in healthcare infrastructure. This encompassed a shortage of hospital beds, healthcare workers, and medical equipment. Numerous studies have highlighted the significant association between healthcare resource availability and the effectiveness of the pandemic responses.

One early study by Bigiani et al. [27], conducted during the initial phase of the pandemic, identified a positive correlation between country-specific COVID-19 death rates and hospital stress, defined as bed saturation. Similarly, Hradsky et al. [28] demonstrated that the organization of healthcare access significantly influenced outcomes in COVID-19 patients, with an inverse correlation observed between death rates and the number of available hospital beds. Expanding on these findings, Mattiuzzi et al. [29] analyzed data across the European Union, revealing that COVID-19 death rates were positively associated with acute care bed occupancy rates and inversely correlated with the number of general hospitals, physicians, and nurses. This underscores that deficiencies in national healthcare systems significantly impacted patient outcomes during the pandemic. Further investigations conducted in the United States [30,31] confirmed that higher numbers of physicians and nurses were inversely correlated with COVID-19 death rates.

An analysis of Italian data by Perona [32] also reinforced these conclusions, demonstrating that fatality rates varied across regions based on healthcare expenditure, system performance, and the availability of hospital beds and physicians. Bed saturation and acute care capacity were identified as critical factors contributing to mortality. Similarly, Castagna et al. [33] found that both the number of available hospital beds and their occupancy rates were significant predictors of COVID-19 outcomes. While overcrowding and strain on the healthcare system occurred in certain regions, a significant issue in some countries like the US was the underutilization of healthcare services. Critical care units and emergency departments were notably underused, as patients with acute cardiovascular emergencies avoided seeking hospital care. This led to a sharp decline in cardiovascular procedures and medication use, resulting in a substantial increase in mortality within the cardiovascular patient population [34,35].

Cumulative evidence from these studies strongly indicates that inadequate preparedness in public health infrastructure and resources significantly exacerbated the COVID-19 pandemic's impact. This highlights the urgent need to establish comprehensive measures for future pandemics, including investing more in healthcare, developing reliable response plans, stockpiling medical supplies, and increasing funding in surveillance systems to respond to emerging threats in a timely manner [36].

2.3. Inadequate Therapeutic Management

Although delayed recognition and lack of preparedness undeniably played a significant role in the inadequate response to the pandemic, additional factors also likely exacerbated the global health crisis, with inappropriate clinical management emerging as a dominant contributor. Several reasons underpin this insufficiency.

A detailed discussion in the previous section highlights the inadequate availability of human and technical resources to address the crisis effectively. However, another critical factor was the limited understanding of the biological implications of SARS-CoV-2 infection, which significantly aggravated the situation [37]. This issue becomes even more concerning given that COVID-19 marked the third major coronavirus outbreak in the past 20 years, following severe acute respiratory syndrome (SARS) and Middle-East respiratory syndrome (MERS) [38]. Many of the clinical deteriorations observed with SARS-CoV-2 infection were already evident in these earlier outbreaks, particularly with SARS [30]. The primary factor that likely constrained the research on highly pathogenic beta-coronaviruses such as SARS-CoV(-1) and MERS-CoV was the relatively low number of infections and fatalities caused by these previous two viruses [39]. These earlier outbreaks were largely limited to small, localized clusters or isolated cases, which may have reduced the urgency and prioritization of research efforts. In summary, the small-scale epidemics and geographic containment that have characterized both SARS and MERS have probably contributed to the lack of extensive investigation into these pathologies, despite their potential to inform responses to future coronaviruses pandemics (like COVID-19).

Delays in comprehending the intricate biological interplay between SARS-CoV-2 and the human host also likely contributed, to some extent, to the elevated case fatality rates observed during the early phases of the COVID-19 pandemic. The leading pathogenetic mechanisms that could only be recognized after several weeks of the ongoing pandemic include immune dysregulation, characterized by hyperinflammatory states such as cytokine storms, which was not initially understood and delayed the deployment of immunomodulatory therapies, along with the systemic, multi-organ impact of SARS-CoV-2, initially mischaracterized as a purely respiratory pathogen. This resulted in an underestimation of its ability to affect multiple organs beyond the lungs, including the kidneys (e.g., acute kidney injury), heart (e.g., myocardial ischemia and myocarditis), liver (e.g., hepatitis), brain and nervous system (e.g., strokes, encephalopathy, Guillain–Barré syndrome), endothelial cells and vasculature (e.g., venous and arterial thrombosis), and the immune system (e.g., lymphopenia and immune dysregulation), along with the significant development of microthrombosis across multiple organ systems, a feature seemingly paradigmatic of COVID-19, which contributes to both the acute and chronic effects of the disease [40]. These delays in recognizing the systemic impact of SARS-CoV-2 impeded the timely application of targeted therapies, including antiviral drugs, corticosteroids, anti-inflammatory agents, and anticoagulants, which are now integral to the management of severe cases.

Then, inadequate and often ambiguous public health communication from governments, international and national health organizations, scientific societies, and individual scientists has contributed to diminishing public trust in scientific authorities. Last but not least, health inequities that have characterized the COVID-19 pandemic have represented an important issue, as disparities in healthcare access, therapies, vaccines, and outcomes were evident across different populations. These inequities were influenced by a vast array of factors, including age, race, ethnic origin, underlying health condition, socioeconomic status, and geography.

2.4. Inefficient Laboratory Response

One of the key challenges highlighted by the COVID-19 pandemic is the difficulty in developing diagnostic tools for detecting novel pathogens. Although the sequence of SARS-CoV-2 was made publicly available early (on 10 January 2020, via the Global Initiative on Sharing All Influenza Data, GISAID), and clinical laboratories quickly began developing in-house tests for the virus [41], the widespread availability of rapid, high-throughput diagnostic techniques was delayed, overwhelming laboratories globally [42]. This issue is not unique to COVID-19, as the diagnostic industry requires significant time to develop, validate, and receive regulatory clearance for tests before they can be commercialized. In line with this, a survey conducted by the American Association for Clinical Chemistry (now the Association for Diagnostics and Laboratory Medicine, ADLM) revealed that, during the early stages of the pandemic (up to July 2020), many US clinical laboratories reported delays of over a week in providing test results to patients, primarily due to shortages of supplies, particularly involving test kits (reported by up to 58% of respondents), reagents (46%), and swabs (28%) [43]. Notably, the survey also found that one-quarter of the laboratories surveyed were unable to perform all the COVID-19 tests requested. A shortage of staffing was also highlighted during the early phase of the pandemic, as over 80% of US laboratories indicated that this aspect was determinant in providing a timely response.

A following survey conducted by the College of American Pathologists (CAP), the American Society for Microbiology, and the National Coalition of Sexually Transmitted Diseases (STD) Directors in 2020 and 2021 provided similar figures, as 69% of responders reported difficulty in acquiring test kits to conduct SARS-CoV-2 testing, 66% reported difficulty in purchasing nasopharyngeal swabs, 60% reported workforce shortages, and 30% reported difficulty in getting personal protective equipment.

While these significant findings undoubtedly support the conclusion that the medical laboratory community was largely unprepared to address this critical challenge, it is clear that the primary cause lies in the underestimation of the essential role of laboratory diagnostics during outbreaks and other natural disasters. It is indisputable that the underfunding of laboratory services has been a longstanding political issue in many countries over the past decades, accompanied by the centralization and consolidation of laboratory services in larger facilities, where economic considerations often outweighed the reliability and clinical efficacy of diagnostic tests [44]. These economic cuts primarily affected laboratory staffing, as professionals were burdened with excessive workloads, stress, and even burnout, so that laboratories faced enormous challenges in their ability to retain or recruit qualified personnel [42–44]. The significant number of SARS-CoV-2 infections among laboratory staff, exacerbated by shortages of personal protective equipment (PPE), further increased absenteeism [44]. Another key factor was the unprecedented demand for COVID-19 testing, which overwhelmed laboratory capacity. Many laboratories were not sufficiently equipped to manage such large volumes, leading to delays, shortages, and further staff burnout [42]. Notably, several laboratories lacked the necessary infrastructure, such as physical space, automation, and high-throughput technologies, to rapidly scale up testing [43,44]. Furthermore, rapid diagnostic tests (RDTs), particularly antigen-based SARS-CoV-2 tests (Ag-RDTs), were unavailable for several months at the onset of the pandemic, a challenge that has been mirrored in the current response to the mpox outbreak [45]. Although the clinical performance of rapid diagnostic tests—particularly their diagnostic sensitivity—is generally lower than that of gold-standard techniques such as nucleic acid amplification tests, they offer several practical advantages. These include the following: (i) the ability to provide results in a very short time (minutes, compared to the hours or days required for molecular tests), enabling the rapid identification of infected individuals; (ii) a user-friendly design, which reduces the need for laboratory access or specialized healthcare personnel; (iii) versatility in deployment across various settings, including remote or resource-limited areas; (iv) scalability for large-scale testing, facilitating mass screening during outbreaks; and (v) a lower cost compared to more complex diagnostic methods.

It is then undeniable that COVID-19 diagnostics not only seem crucial for detecting SARS-CoV-2 infections, but also offers several additional advantages, such as aiding in the prediction of future testing demand [46], monitoring the evolution of local outbreaks [47], enabling the more timely identification of new variants and the reliable estimation of their prevalence among the general population [48], potentially anticipating the progression of new cases, COVID-19-related hospitalizations and deaths several days in advance [49,50]. It is also noteworthy that, although certain areas experienced shortages, others faced issues of oversupply, highlighting that achieving balance was another primary challenge.

It is therefore indisputable that the lessons learned from the COVID-19 pandemic should inform governments, hospital administrations, and laboratory professionals in enhancing preparedness for the potential risk of another global catastrophe. This can be achieved by implementing a series of interventions, such as those summarized in Table 1.

Table 1. Interventions to enhance the level of alertness and preparedness of laboratory medicine to face a new potential worldwide catastrophe.

• Increased investment on laboratory infrastructure, instrumentation, and workforce. • Strengthened laboratory networks. • Accelerate the development, clinical validation, and clearance of new diagnostic tests.
• Invest more on rapid and scalable diagnostic tests

3. Conclusions

The COVID-19 pandemic has exposed significant inadequacies in healthcare systems worldwide; yet, it represents only one of the many emerging threats that may challenge global health in the future, and we should also use these lessons to consider future countermeasures for the issue of long-COVID [51].

The shortcomings revealed during the COVID-19 pandemic underscore critical areas that require substantial improvement to ensure more effective responses to future health emergencies. These areas of concern are briefly summarized in Table 2, which were identified based on both our personal experience and the prominence they hold in the literature reviewed in our article. Notably, the impact of the pandemic has varied across regions, geographic areas, and health systems, with certain strategies proving more effective than others in specific contexts. This article aims to propose a series of evidence-based recommendations to enhance preparedness for future pandemic risks.

Table 2. Key areas in need of improvement to ensure more effective responses to future health emergencies.

- Improving and strengthening health information
    - Strengthen international collaboration;
    - Enhance and improve real-time data sharing and integration;
    - Develop and regularly update global health surveillance networks.
- Pandemic preparedness and response planning
    - Sustain investments in healthcare;
    - Development of comprehensive contingency plans;
    - Stockpiling personal protective equipment, medical and laboratory supplies;
    - Strengthen supply chains;
    - Expand healthcare infrastructure to especially increase capacity for critical care.
- Develop a resilient healthcare workforce
    - Prevent shortage of healthcare staff;
    - Train, support, and protect the healthcare staff;
    - Establish pathways to timely mobilize and deploy the healthcare staff;
    - Recognize the importance of mental health programs to prevent or manage excessive stress.
- Invest more in research and development
    - Fast development, clinical validation, and clearance of diagnostic tests, therapies, and vaccines;
    - Continue to study the biology of pathogens.
- Expand the use of telemedicine and digital health
- Allow universal access to healthcare
- Improve public health communication and trust
    - Provide clear, trustable, and consistent messages to the public;
    - Combat misinformation

It is important to mention here that some steps in the right direction have already been undertaken. For example, the WHO has launched a new initiative, called Coronavirus Network (CoViNet) [52], which aimed to collect experts in human, animal, and even environmental health for monitoring of already existing coronaviruses (e.g., MERS-CoV and SARS-CoV-2), and especially to allow early identification of novel pathogens that may pose a serious hazard to human health. However, further efforts are required to create a safer world and to identify critical aspects of human biology and physiology—such as obesity, one of the most prevalent risk factors [53]—that significantly influence the biological response to pathogens.

This perspective article, mostly based on personal experiences of the COVID-19 pandemic, may not encompass all aspects or evidence that potentially hindered an effective response. However, many of these issues have been extensively addressed in other publications within this journal [54–56], and are, hence, beyond the scope of our analysis.

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