

## Insights and pearls of healthcare systems management of COVID-19 in Asia and its relevance to Asian transplant services

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Asia is now the new epicenter of the coronavirus disease 2019 (COVID-19) pandemic, yet mortality rates remain among the lowest in the world. This review paper summarizes key findings from the literature in Asia on how healthcare systems, including transplant programs, have developed innovative solutions and countermeasures to mitigate the adverse impact of the COVID-19 pandemic. A review of literature using PubMed was performed, where only publications addressing COVID-19 and healthcare systems from Asia were selected. Whenever possible, the impact of COVID-19 and the countermeasure responses from transplant healthcare systems were highlighted in these publications. Transplantation in Asia has been affected to varying degrees, although many Asian countries have continued transplantation while adopting defenses that have resulted in a low COVID-19 incidence rate among transplant recipients. These defenses include protected pathways for patients, surveillance through protocol screening for COVID-19, team and infrastructure segregation, adoption of telemedicine, and patient outreach and education. Transplant healthcare systems in Asia have been effective at varying levels of success during the COVID-19 pandemic. As the pandemic continues, transplant healthcare systems must develop operational frameworks to sustain transplant activity in the new normal.

**Keywords:** COVID-19; Asia; Transplant healthcare systems

### INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic caused by the severe acute respiratory syndrome coronavirus 2 virus (SARS-CoV-2) has passed more than 18 months since the World Health Organization declared the pandemic on March 11, 2020. Since then, the world has struggled to adapt and mitigate the impact of a virus that is proving to be highly adaptable and difficult to eradicate. This is especially felt in Asia, where it is now the new epicenter of COVID-19 with the highest cumulative number of

COVID-19 cases compared to other regions in the world. Despite this, the mortality rate due to COVID-19 was reported to be among the lowest in the world at 1.1% compared to 1.49% in North America and 1.76% in Europe [1].

Although this observation has not been systematically analyzed in detail, it can be postulated that the lower death rates from COVID-19 in Asia may be attributed to a younger population, which, as a result, has fewer comorbidities and is more likely to experience less severe COVID-19 [2]. Furthermore, many Asian countries have developed pandemic response systems that could be activated at short

## HIGHLIGHTS

- There is a paucity of data from Asia on how healthcare systems especially those in transplantation are responding to the challenges of coronavirus disease 2019 (COVID-19).
- Unique discoveries and solutions have arose from various countries in Asia which can be adapted into transplant services in Asia.
- Despite high caseloads of COVID-19 in different countries from Asia, the incident rate among transplant recipients have remained low because of effective defensive measures taken by transplant programs in Asia.
- As the COVID-19 pandemic continues into another year, transplant healthcare systems must develop operational frameworks that are responsive to changing prevailing conditions of COVID-19 in order to sustain transplant activity in a new norm.

notice in the event of a new pandemic [2]. Finally, wearing masks in many Asian countries is considered acceptable even during non-pandemics, and Asian societies are generally more willing to adhere to social distancing measures to prevent the further spread of COVID-19 [2].

It then begs the question of whether the impact of COVID-19 on transplant healthcare systems has been similarly blunted, and this paper intends to review the available literature from Asia regarding this, focusing on what is known and being implemented one year after the pandemic has been declared.

## COVID-19 COUNTERMEASURES IN ASIA

Some countries have performed well in flattening their COVID-19 curves and, more importantly, in protecting their healthcare systems from being overwhelmed, which was the case in China, Italy, North America, and India. In the Asia-Pacific region, there are five important factors that seem critical in flattening the COVID-19 curve [3]. These factors include the following: (1) early border closures with testing and quarantine of visitors; (2) mandatory notification when COVID-19 is diagnosed to accurately monitor the magnitude of the outbreak; (3) aggressive contact tracing and early quarantine to minimize the formation of

large clusters and spread to other parts of the country; (4) building COVID-19 testing capabilities and using them in a pre-emptive manner to detect pre-symptomatic and asymptomatic cases; (5) decisive government leadership and integrated national approach using multi-ministerial task forces; and (6) most importantly, cooperation from the general population with masking up and social distancing facilitated by government financial support for those economically affected by COVID-19 related restrictions.

These measures have been implemented with significant success in countries such as Taiwan, New Zealand, Vietnam, and Singapore. These countries have been effective enough to flatten their COVID-19 curves following initial outbreaks. Unfortunately, with the relaxation of border closures and reopening of economies, some countries like Taiwan and Vietnam are now experiencing recurrent and intense waves of COVID-19 exacerbated by more contagious variants of COVID-19 and sluggish vaccination program across many countries.

## PEARLS OF COVID-19 FROM ASIA

In an observational study from Hong Kong, Japan, Singapore, Taiwan, Thailand, and Vietnam, early COVID-19 work-related cases commonly affected those working in the sales and transport industry in the first 10 days following the first locally transmitted cases [4]. However, in the later period, extending to 40 days from the first locally transmitted cases, healthcare workers (HCWs) form the majority of those infected. Furthermore, 95% of HCW infections had a clear and traceable contact history with a confirmed case of COVID-19. Thus, it is clear that HCWs are very vulnerable to infection with SARS-CoV-2. When China was the epicenter of the COVID-19 pandemic in the beginning of 2020, the Chinese healthcare system was caught unprepared, resulting in thousands of HCWs being infected [5]. Significant nosocomial transmission occurred and was driven by many factors such as (1) lack of recognition of COVID-19 syndrome, (2) lack of point-of-care diagnostic assays, (3) lack of awareness to take precautions, (4) inadequate training and shortage of personal protective equipment (PPE), and (5) lack of disclosure by patients on their exposure history. These were valuable lessons that were rapidly taken up by healthcare systems in Asia to blunt the impending waves of COVID-19 infections that were to hit upon them weeks to months after the initial epidemic in China.

Although PPE is now accepted as a necessary defense against COVID-19 infections in HCWs, it should not be restricted to those dealing with only confirmed cases because COVID-19 may present with symptoms that are associated with more commonly encountered diseases such as dengue in Southeast Asia, which do not require PPE. In Singapore, it was reported that patients who presented with dengue fever-like symptoms supported by positive dengue serology were found instead to be COVID-19, while the dengue polymerase chain reaction was negative [6]. This phenomenon has also been reported in Thailand, and in one report, resulted in transmission of COVID-19 to a nurse who was not wearing PPE while caring for the patient [7].

To reinforce the point that COVID-19 may not initially be suspected can also be inferred from a large cohort study from India, where 6% of kidney transplant recipients were asymptomatic, while 24% presented with diarrhea [8]. Furthermore, 49% of the study population had normal chest X-rays at the time of presentation. This suggests that perhaps when COVID-19 is significantly prevalent in the community, all transplant patients should be screened for COVID-19 when they are admitted to the hospital. The potential advantages of such a screening strategy would be to identify unsuspected cases early before they can cause nosocomial transmission in a hospital unit. In fact, hospitals in Singapore adopted this strategy by converting an allocated number of inpatient wards to respiratory surveillance wards (RSWs) [9]. This represented a containment strategy in which patients with respiratory symptoms, febrile syndromes, or diarrheal illnesses were admitted to RSWs. In these RSWs, staff were on heightened alerts wearing full PPE, and there was a screening protocol to swab patients for SARS-CoV-2. Furthermore, cohort rooms had their bed capacity reduced from four–six to three to ensure adequate social distancing between patients who needed to wear a mask. The Singapore General Hospital reported its experience with this approach during a 6-week period in which 1,178 patients were admitted [9]. Interestingly, about 1% of this cohort were screened positive for SARS-CoV-2, which enabled their quick transfer to isolation wards, averting nosocomial outbreaks. Another advantage of this containment and screening strategy is the reported eradication of hospital-acquired respiratory viral infections [10].

It is widely accepted that COVID-19 may present as asymptomatic or pre-symptomatic infections in transplant recipients, with an incident rate of 4%–5% [8,11]. Hospi-

tal staff have also been found to be asymptomatic for COVID-19. A U.K. study reported that 3% of individuals in a large teaching hospital tested positive for SARS-CoV-2 in the absence of symptoms [12]. Given that nosocomial outbreaks can be potentially devastating, especially with more contagious variants in circulation, this raises the possibility of a role for routine screening of all HCWs and patients regardless of their COVID-19 risk level. Indeed, at least in Singapore, this has been the approach in which all inpatients and staff are regularly swabbed for SARS-CoV-2. In one report from the Singapore General Hospital, 0.13% (n=17/13,066 staff) screened positive for SARS-CoV-2 [13]. In addition, screening becomes more critical if there are active COVID-19 clusters in proximity to hospitals. For example, seven HCW and 20 inpatients tested positive for SARS-CoV-2 during a 6-week period at the Singapore General Hospital, 52% of which were linked to a large active community cluster near the hospital [13].

In the earlier understanding of SARS-CoV-2 transmission, it was widely believed that respiratory droplets were the dominant route of transmission and that it was not an airborne disease. However, data from Malaysia now suggest that COVID-19 could be an airborne disease under specific circumstances, such as enclosed spaces with recirculation of air. In one of the Malaysian studies, SARS-CoV-2 RNA was detected from a particulate matter of size 2.5  $\mu\text{m}$  or less in a single room ward, as well as one cohort room where the air sampler was located far away from air filtration devices [14]. However, the study was unable to perform viral cultures to confirm that the RNA detected was from viable viruses. Nevertheless, this suggests that airborne viral particulate matter may be dispersed in enclosed environments such as hospital wards. In a second Malaysian study, computational fluid dynamics were used to track the dispersion of exhaled particles from a patient in an enclosed air-conditioned space under different exhalation conditions and different flow rates [15]. The study reported that exhaled particles are dispersed in the ward, enhanced by air flows generated by air conditioners. Furthermore, particulate matter could be detected beyond 1 m of the patient bed, suggesting that safe distancing measures of 1 m or more may not be sufficiently protective. This would raise concern that in enclosed spaces such as inpatient wards, SARS-CoV-2 could spread by the airborne route. As a result, hospitals from Asian countries such as Taiwan and Singapore have retrofitted exhaust fans to move air outwards from the inpatient ward and open windows to improve ventilation [16].

**Table 1.** Defensive measures against COVID-19 by Asian transplant healthcare systems

Domain	Countermeasure
Donor management	Donor screening for exposure risk factors, COVID-19 screening through swabbing and chest radiology, preoperative isolation of living kidney donors
Recipient management	Recipient screening for exposure risk factors, COVID-19 screening through swabbing and chest radiology, preoperative isolation of transplant recipient
Transplant program activity	Continuity of transplant program activity adjusted to the national COVID-19 prevalent situation and availability of healthcare resources to perform transplantation
Surgical precautions	Separation of organ procurement and implantation team, dedicated operating theatres for transplant surgeries
Post-operative management	Isolation of living donors and transplant recipients, dedicated post-operative transplant teams, ensuring availability of PPE
System processes to mitigate COVID-19 spread	Hospital perimeter screening for visitors and patients at risk for COVID-19, fever detection stations, mandatory mask-up in healthcare facilities, social distancing measures, restriction of healthcare workers between hospitals, restriction of movement of healthcare workers, screening of inpatients and staff for SARS-CoV-2

COVID-19, coronavirus disease 2019; PPE, personal protective equipment; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2 virus.

### ADAPTING TO COVID-19 IN TRANSPLANT HEALTHCARE SYSTEMS IN ASIA

Organ donation and transplantation in Asia have been adversely affected by the COVID-19 pandemic but to varying degrees. Most countries had elected to shut down transplant services, but some countries permitted deceased donors and urgent transplantation to continue, such as Hong Kong, Malaysia, and Singapore [17]. Noticeably, South Korea had most transplant programs remaining active during this time, which may account for the high rate of transplants being performed during the first 3 months of 2020 [18]. As the pandemic continues for another year, it would be unsustainable for transplant programs to keep suspending services, as this would have an impact on the mortality of transplant candidates. For example, in the United States, the kidney transplant waiting list mortality was higher during the COVID-19 pandemic [19]. As a result, transplant programs in Asia could adopt a dynamic framework to facilitate decision-making on the functioning levels of transplant services that could be fluid and responsive to the changing COVID-19 climate [20]. The framework included considerations on the prevailing knowledge of the pathogen and pandemics, risks and benefits of one treatment over another during a time when the risk of COVID-19 exposure was high and what management options were available to mitigate the risks of COVID-19 infection. Such a framework could be integrated into a country's national outbreak response system, and transplantation services

could be scaled up or down according to the prevailing COVID-19 situation in a particular country [21].

In addition to transplant healthcare systems' considerations in determining the level of transplantation activity, healthcare leadership should also consider the willingness of transplant candidates to be transplanted during the COVID-19 pandemic. In a survey of transplant candidates from Singapore, most waitlisted candidates recognized that the current pandemic is a serious situation affecting their care and that COVID-19 poses a significant risk to health [22]. Despite the increased risks, most patients reported that they would choose immediate transplantation if there was no foreseeable end to the pandemic, especially if the medical urgency did not permit further delays. Finally, there is reassurance that the rate and mortality of COVID-19 infections in transplant recipients in Asia appear to be low [8,17]. This could be related to the pre-emptive defensive measures adopted by Asian transplant programs for their patients during this period, which was consistent across different Asian countries (Table 1) [17]. In one report from a transplant center in Singapore describing countermeasures against COVID-19, no deaths or graft loss were reported among kidney transplant recipients during the initial wave of COVID-19 infection [23]. In addition, the mortality of wait-listed patients did not increase, contrary to the observations from the United States [23].

Nevertheless, there were certainly challenges faced by Asian transplant programs during the COVID-19 pandemic. These included the (1) limited availability of COVID-19

testing, (2) reduced access of patients to hospitals and medication supplies, (3) diversion of transplant manpower to COVID-19 frontlines, (4) reduced supply of blood products due to reduced donations, and (5) frequent rejection of potential organ donors due to suspected exposure or positive testing.

## CONCLUSION

Although Asia was the first to be affected by COVID-19, it has not witnessed high mortality, and many Asian countries have been able to flatten their COVID-19 curves through effective system and community countermeasures. Unique experiences and innovative solutions have emerged in Asia to mitigate the adverse impacts of COVID-19, with some success. Finally, transplantation in many Asian countries has continued at varying risk-stratified levels without experiencing high COVID-19 infection rates in transplant recipients. With sluggish vaccination rates and the emergence of new SARS-CoV-2 variants, transplant programs in Asia will need to adapt to an endemic COVID-19 world and adopt system frameworks that can guide the level of transplantation according to prevailing infection rates in the country.

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### Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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