A Comprehensive Review of the Cross-Disciplinary Impact of COVID-19 in India

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Abstract:

A novel coronavirus (2019-nCoV) responsible for a severe acute respiratory disorder (SARS-CoV-2) in humans, with its epicentre in Wuhan, China emerged in December 2019. This coronavirus, by far, has hit >200 countries, affecting 7 million worldwide accounting 11% death of the affected population. The transmission is majorly caused by human-to-human contact and, through fomite. In view of the increasing number of COVID-19 cases and the absence of definitive treatment or vaccinations, WHO has deemed the viral infection a pandemic of international concern. In such grave situations, there is a need for expanding the health sector workforce, government and police workforce, sanitation and prevention strategies. The current article describes the virology aspect, control of COVID-19 and revisits the various treatment options available at present this deadly infection. Epidemiology of COVID-19 is also discussed to further understand the pandemic status of India. The article also discusses implicating quarantine or social distancing, and in extreme cases, lockdown or alternative approaches such as herd or indirect immunity, as a measure to control the pandemic. Lockdown or social distancing will give rise to economic, emotional, political and social downfall in the country. It is estimated that a lockdown period will set back the country, possibly, by $240 billion, yet it stands unavoidable in the spread of control of infection. Thus, policymakers should strategize economic revival depending upon the best possible data and critical understanding.

Introduction

With the initial discovery of novel fatal coronavirus SARS-CoV-2 causing acute respiratory infection COVID-19 in humans in Wuhan, China, a pandemic arose affecting approximately 7 million worldwide and accounting for 11% death of the affected population. The virus is found in more than 200 countries, amongst which leading nations are USA, Italy, Spain, Germany, France, India followed by China with 80,000 cases and counting [Worldometer, Coronavirus]. This has taken a toll on world's economy. The death toll due to 2019-nCoV has already surpassed the acute respiratory syndrome SARS-CoV 2003 and Middle East respiratory syndrome MERS-Cov 2012 outbreak combined [Srinivas et al., 2020]. The mode of transmission of SARS-CoV-2 is similar to MERS-CoV that is human-to-human and though reported, zoonotic source of transmission is an uncommon event [Altamimi et al., 2020]. On January 30, 2020, the

WHO declared SARS-CoV-2 epidemic a health emergency of international concern. Similar situation was tackled in past with MERS-CoV with respect to discovery of a fatal infectious viral strain, uncertainty of its origin and transmission, invariable and irreversible threat to global economy [Zumla and Memish, 2014]. However alarming this situation might appear, discovering vaccination and treatment might take months or even years. The purpose of this review article is to provide researchers with a platform to find intricate information on this novel coronavirus.

Expected Origin and Structure:

Innovative Vector Control Consortium (IVCC) named the novel beta-CoV as SARS-CoV-2. Sequence analysis suggested that 2019-nCoV possesses a genome that belongs to Betacoronavirus genus and is closely related to bat-SL-CoV ZC45, bat-SL-CoV ZXC21 and is distantly related to SARS-CoV. CoVs belong to subfamily of Coronavirinae in the family of Coronaviridae of the order Nidovirales. Genome of CoVs is a single stranded positive-sense RNA (+SSRNA of 30Kb) with 5'-cap and 3'-poly-A tail [Wrap et al., 2020, Chen.Y. et al., 2020]. The Genomic characterization has revealed that bats and rodents are source of alpha and beta CoVs and avian species seems to represent delta and gamma Covs [Cascella et al., 2020, Rodriguez-Morales et al., 2020, Adhikari etal., 2020]. Recent reports suggests that virus isolated from *Rhinolophus affinis* and infected human strain SARS-CoV-2 shows 96.2% similarity whereas, pangolin virus isolate shows 99% similarity suggesting pangolin to be a more likely intermediate host of SARS-CoV-2[Xu et al., 2020].

The genome of SARS-CoV-2 is similar to that of typical CoVs. It contains at least 10 open reading frames (ORF), about 2/3rd of the viral RNA is translated in to two large polyproteins and non-structural proteins (nsp) enabling viral replication and transcription. On the other hand, remaining 1/3rd codes for four main structural proteins Spike (S), Envelope (E), Nucleo-caspid (N), Membrane (M) proteins and other accessory proteins with functions not discovered yet[Li et al., 2020]. S protein is thought to be involved in host tropism by recognition and attachment to receptor angiostensin-converting enzyme 2 (ACE2) on the outer host cell membrane [Tilocca et al., 2020, Shereen et at., 2020]. NSPs which is 58% of the viral genome are found to be conserved and implies dependence on structural proteins to invade new hosts. [Ketkar et al., 2020]

History and Epidemiology of COVID-19

2019-nCoV is by far the seventh in family of coronaviruses [Lin et al., 2020] that infects humans and animals with manifestations as respiratory, enteric, hepatic and neurological diseases [Liu et al., 2020, Biscayart et al., 2020].

The first phase began on 29th December 2019 where the first case was detected in China. Initial infection was thought to be contracted by humans through Huanan seafood market in Wuhan, China, as 27 of the initial 44 cases were exposed to this market. Chinese Center for Disease Control and Prevention (CCDC) suspected that this infection was related to wild-life trade. However, further inquiries revealed that there were few patients who had not been to Huanan seafood market nor had a travel history to Wuhan, thereby suggesting human-to-human spread of COVID-19. By 13th of January, 41 cases were confirmed in China suggesting human-to-human contact transmission [Zhou et al., 2020, Fan et al., 2020].

After this, the second phase started with patients being discovered with COVID-19 outside China and Thailand. On 22nd January, about 571 individuals in 25 provinces of China were infected with COVID-19 thereby, pushing Wuhan to implement a state of lockdown. As of 2nd February 2020, more than 14,000 individuals contracted SARS-CoV-2 with 300 deaths in China [Pan et al., 2020].

Outbreak of 2019-nCoV causing pandemic was predicted earlier by Zhang, L et al, in early February of 2019 [Zhang et al., 2020].There was a rapid increase in the cluster of cases which takes us to the third phase of COVID-19. Within a month on 30th January 2020 the number went to 7734 along with its infection being spread to other countries as U.S reported its first case on 30th January 2020 [Rothan et al., 2020]. The epidemiology curve thus, can be roughly divided into three phases: 1. Occurrence of affected individual, 2. Infection to a new individual due to contact with individual with travel history to affected countries, and 3. Affected patients withh no contact with affected individuals (outbreak where the source in untraceable) [Sun et al., 2020].

Symptoms, Clinical Features and Diagnosis

General clinical manifestations of COVID-19 are throat irritation, fever, diarrhea [Lo et al., 2020] followed by subsequent decrease in white blood cells and imaging characteristics of pneumonia-like respiratory related symptoms. Clinically, patients suffering from COVID-19 may present elevated levels of C-reactive protein, ESR, lactate dehydrogenase, creatinine and prolonged prothrombin duration [Sohrabi et al.,

2020]. The ACE-2 receptor on the host cell membrane that is responsible for viral entry in to the host, has also been implicated in cardiovascular diseases (CVD). When compared with normal individuals, patients with CVD show exacerbated symptoms [Zheng et al., 2020]. However, 1% of the cases of COVID-19 patients in China were tested positive even in absence of any peculiar symptoms [Wu et al., 2020]. Additionally, clinical features of secondary hemophagocytic lymphohistiocytosis (sHLH), which is triggered by viral infections, are unremitting fever, cytopenias and hyperferritinamea. Cytokine profile similar to sHLH is associated with COVID-19 disease and is characterized by increase in IL-2, IL7, granulocyte colony stimulating factor, interferon-γ inducible protein, monocyte chemoattractant protein, macrophage inflammatory protein 1-α, and tumour necrosis factor-α. Recent report on a multicentre study of 150 confirmed COVID-19 patients in Wuhan, China, revealed elevated ferritin (mean 1297·6 ng/ml in nonsurvivors vs 614·0 ng/ml in survivors) [Mehta et al., 2020]. Radiological findings of 81 patients in Wuhan China suggested that COVID-19 pneumonia shows Chest CT imaging abnormalities even in pre-symptomatic phase of the infection.

Thus combination of clinical, laboratory and imaging findings should serve a proper early diagnostic tool for detecting COVID-19 patients [Pan F et al., 2020]. Infection is simultaneously diagnosed with the aid of real-time fluorescence polymerase chain reaction (qRT-PCR) of fluid from bronchoalveolar lavage [Sohrabi et al., 2020, Shi et al., 2020].

Treatment of COVID-19:

Chloroquine phosphate has shown apparent safety and efficacy against COVID-19 in multicentre clinical trials. [Gao et al., 2020]. According to 23 ongoing trials in China, Chloroquine was found effective in limiting replication of SARS-CoV 2 [Colson et al., 2020 Cortegiani et al., 2020, Touret et al., 2020]. About 20 patients treated with combination of Hydroxychloroquine and Azithromycin showed reduced viral load after 6 days of treatments [Gautret et al., 2020 and Colson et al., 2020] .

Convalescent plasma therapy is yet another treatment suggested for managing COVID-19. Patients receiving neutralizing antibody along steroids and mechanical ventilation showed improved clinical status. Another report that recommended removal of corticosteroids to manage COVID-19 patients, also suggested to test efficacy and safety of plasma therapy In a review article, convalescent sera was suggested as an option for containing SARS-CoV-19 spread among the families of patients or medical workers. [Shen et al., 2020, Chen. L. et al., 2020, Casadevall et al., 2020]. A recent article by Keith, et al,

April 2020 suggests randomized trials are required to be designed to check the efficacy of therapeutic plasma exchange in the treatment of COVID-19. [Keith et al., 2020]

IL-6 Cytokine has implication in inflammation during COVID-19 ARDS and hence its interference may be therapeutic in nature. Tocilizumab, an IL-6 blocker helped alleviate clinical manifestation such as decrease CRP, good prognosis and repressed deterioration of severe COVID-19 patients [Xu X et al., 2020].

Thalidomide along with low glucocorticoids has shows implications in inflammatory cytokine surge inhibitory effects, alleviating anxiety to reduce oxygen consumption, and relieved lung exudation [Chen C et al., 2020].
A case study on Lopinavir / Ritonavir revealed that a 54 y/o patient showed reduction viral road however in another trial conducted with 99 patients no significant benefits were observed. [Lim et al., 2020, Cao et al., 2020, Baden et al., 2020]

Anti-malarial drugs, anti-viral drugs, convalescent plasma therapy, and cytokines have been used to manage and treat COVID- 19. However the uncertainty of the efficacy of these drugs across the globe, age-related discrepancies and prevalence of co-morbid situation has led into adopting preventive or control measures to spread the infection.

Rationale to Implementation of preventive measure for COVID-19 infection in India
As of now, no vaccine has been developed for SARS-CoV-2. So the best way to deal with this situation is proper protection and sanitation, identifying early indications of the disorder, early and quick diagnosis, reporting, and supportive treatment [Sun P. et al., 2020]. Reports have suggested that it is important to identify persons with few or no clinical symptoms as they may later develop COVID-19 infection [Yang et al., 2020]. With increasing number of COVID-19 patients, the prevention strategies adopted by the early affected countries were social distancing and subsequent lockdown [Mizumoto et al., 2020]. The human-to-human transmission was identified in two broad contexts: sporadic cases among travelers and patients who acquired infection subsequently through local transmission [Spiteri et al., 2020]. Such rapid transmission suggests other countries to adopt and implement prevention strategies such as avoidance of mass gatherings, social distancing, and lockdown if the situation worsens.

Majorly prevention strategy lies in the essence of identifying unreported cases. Reporting and spread of COVID-19 amongst travelers depends on the following categories of travelers ; 1. symptomatic but unaware, 2. aware of exposure but shows no symptoms, 3. symptomatic and aware, and 4,neither symptomatic nor aware [Gostic et al., 2020].   The patients which fall under category 3 and 2 are major incubators of the virus who can promote its spread within the community consequently infecting non-travelers [Zhao et al., 2020] . However, category 1 and 4 patients intensify difficulties in prevention and management of COVID-19 [Lu et al., 2020]. In one study it was found that the serial transmission intervals were shorter than the incubation period of the virus suggesting that pre-symptomatic transmission had occurred. Hence, the detection of pre-symptomatic individuals with COVID-19 is highly warranted to prevent the spread of infection [Tindale et al., 2020]. The latent period, thus, has a key impact on controllability of COVID-19 making social distancing an inevitable way of slowing the pandemic [Kretzschmar et al., 2020].

Coronavirus and India:

Epidemiology of COVID-19 in India

Correlating the epidemiology of this disease in China to India (Figure 1.), India has began to enter the third phase of this infection. In this third phase, contact history of newly affected individuals cannot be traced back to affected patients with travel history or healthcare workers. After partial lockdown in China the spread of infection measured by R_O, fell below one within two weeks period. According to a preprint published on 2nd April 2020 by Ranjan, it was estimated that the outcome of social distancing would have been evident by reduction in reported cases in India from April 8th, however the prediction model for estimating the patient pool for any country may be affected by violation of quarantine norms [Ranjan et al., 2020]. According to Ministry of Health, India, if a person carries this virus without observing any quarantine, he (or she) is capable of infecting 406 individuals within 30 days, however, following social distancing this number can be brought down to 2.5 individuals. Previous reports suggest that travelling, improper sanitation and precaution can spread this disease beyond control. Unfortunately 2,46,628 cases have been confirmed by far till 7th May 2020. This reinforces the position of social distancing and calls for strict action in case of violation of rules. Minimum activities in India looks inevitable to control spread of COVID-19 across the country.
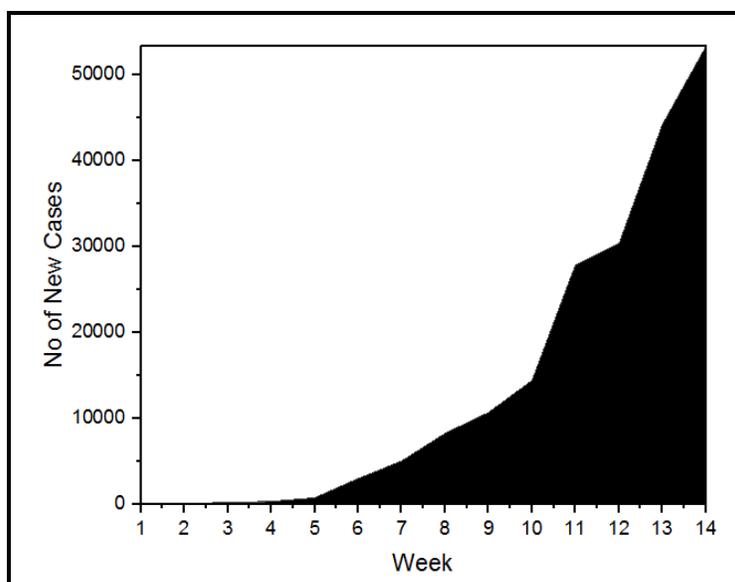
Figure 1: Epidemiology Curve for India (March 1 - June 2, 2020)

Spillover of COVID-19 on Indian Economy

Lockdown and social distancing are bound to bring a huge toll on the economy of the country. The impact of COVID-19 on economy of India has been worst since 1991 due to the efforts of the Government of India to contain the virus. Economically disrupting, the nation is expected to lose over ₹32,000 crores (US$4.5 billion) every day during the first 21-days of complete lockdown. This may lead to financial meltdown in unprecedented ways [Hindu Business Line 2020., Dev et al., 2020]. Consequences of social distancing and lockdown, are temporary shutting down of travel and tourism sector; labor intensive sectors like construction, transport and manufacturing of non-essential items; exports; and supporting sectors like electricity. Lower global demand and price realization will also have an impact on commodities like oil and gas, metals. It might also lead to erosion of purchasing power due to pay-cut, slowdown domestic demand, and ultimately trickle-down effect of demand which will have a longer-lasting impact on some other sectors [Ozili et al 2020., New 18 Business, 2020]. Simplistic solution to measure consequence of COVID-19 and lockdown on Indian economy is to compute loss in economic activity on a daily basis. Pre-COVID-19 projections of average daily India's GDP FY2021 is estimated to be $8 billion and the current 30-day (March-April) lockdown has set the economy of the nation back by possibly $240 billion [The Economic Times, April 3rd 2020]. A recent forecast economists warns that India will face worst recession in 40 years and the economy will shrink by 5% during the current financial year [The Economic Times, May 29th 2020]. Additional trade impact of the coronavirus epidemic on India is

estimated to be $348 million and India stated among top 15, most affected countries due to COVID-19 slowdown, consistent with a UN report [Koshle et al., 2020]

However the world is at a crossroad and COVID-19 pandemic have made people aware of the dependency of humans on one another. The world have faced global economic crisis in the past viz., Wall Street crash of 1929, OPEC oil price shock of 1973, and 1991 Indian Economic Crisis. The International Labour Organization (ILO) had described coronavirus pandemics as " The worst global crisis since World War II" and ILO New Delhi, have predicted increase in global unemployment by around 25 million [ILO, 2020]. The COVID-19 economic crisis is an inevitable event, but not unmanageable and demands protection of economy. This can be implemented by first and foremost focusing on the thumb rule of saving life, followed by estimation of resultant financial damage, and preparing for its subsequent recovery [McKee and Stuckler et al., 2020].

Impact of ' Virality of Virology' on India

India faced the longest COVID-19 national lockdown in the world which has been extended to May 31st 2020. India adopted safety measures like contact tracing, restricted mobilization and extensive testing in a 'toughly and timely' manner which also WHO praised [Lancet, 2020]. However, governments' sudden implementation of lockdown sent a wave of paranoia amongst the immigrants with informal economical background. Since a novel infection, Covid-19 has caused fear, stigma, confusion, and anxiety leading to political, religious and social imbalance in the country and worldwide [Lancet, 2020]. Ideally, this situation calls increased attention from political, industrial and medical sections towards strengthening the healthcare sector of the country. The overwhelming reports from media like news, or social media handles has created disorder in the minds of people all over the world. Social media, which is trying to keep us all informed about COVID-19 situation across borders, has added to distress amongst the people of India [Roy et al., 2020]. More than virology, 'virality' has spread more information and misinformation in India and thus, the first and foremost modus operandi should be control of letting false information go 'viral'. Social media should be harnessed to support public health response, provide public mental support, spread awareness about the disease and gather information on violation of government policies amidst COVID-19 [Depoux et al., 2020]. There is a need of mental strengthening and creating awareness about the actual underlying cause of the infection, risk factors and creating and following one common platform to deliver information related to COVID-19.

This pandemic may lead to emergence of a new India, where the country will manage threats, social and cultural influence on coping, behavior, science communication, decision-making, leadership and empathy. Misplaced anxiety among masses can be managed by only reporting the serious cases or death and not the nearly immune people infected with COVID-19. Discrimination and avoidance of scapegoat groups should be reduced which may globally reduce racial and ethnic prejudice [Van et al., 2020]. In absence of treatment or vaccines available in this pandemic, behavioral changes as risk perception forms the basis of control of spread of COVID-19 infection and at this stage individual behavior is of utmost importance. [Everett et al., 2020]. Many are suffering from non-health related side effects of COVID-19 [Betsch 2020]. Networking among people such as electronic or social media can be utilized for spreading information on 'Harmful and Beneficial' measures to the groups of low-risk perceptions reinforcing importance of hand washing, social distancing, covering mouth and nose while coughing or sneezing. Media should let affected ones deliver information on control measures and their mental status as they have experienced it firsthand [Van et al., 2020]. New healthcare policies should be developed which can address problems like risk equalization in terms of common rate for treating COVID-19 patients. The healthcare sector should also pay attention towards empowering primary care as this sector is under-funded (1.28% of GDP) in India [Lancet, 2020].

India and Impact of COVID-19 on Education:

'Education' is one of the strongest predictors of health and wealth of a country as impact of long term closure of schools will affect the mental state of children who will be returning after a long hiatus due to COVID-19 lockdown [Viner et al., 2020]. School has a major impact on life of every individual. School routine is works as a sort of a coping mechanism for most youngsters with mental issues or special kids with autism who experience anxiety, depression when their schedule is disrupted. Educational institute closure has impacted more than 80-91% of the world's student population [Pragholapati 2020, Van Lancker & Parolin, 2020].

Not much can be anticipated about the mental health effects of COVID-19 on the young and adolescent minds. There is, thus a need to monitor their behavior and attitude towards 'stay at home' and check how their well-being is affected amidst this COVID-19 [Gao, J et al., 2020]. Upon the decrease in rise of cases on every day basis, measures can be taken for relieving lockdown in certain sector, but reopening schools is one of the most difficult decisions. In such cases it is important to examine countries that never implemented closure of schools during the pandemic [Viner et al., 2020]. Long-term alternative form of

learning should be adopted to educate students in the current pandemic situation. Conducting physical examinations is difficult specifically for courses which require on-campus practical sessions. This situation should be considered as an opportunity to come up with innovative ideas to educate the youth of the society and revolutionize education system as a whole.

India, COVID-19 and Policy Making

Non-communicable conditions such as cancer, heart stroke, depression and mental disorders accounted for 47% of global burden of diseases back in 2002 which was predicted to go above 60% by the end of 2020 [Epping-Jordan et al., 2005]. India has experienced epidemiological transition due to constantly changing disease pattern, improved health, socio-economic and nutritional status and eradication of major diseases. However the national burden of diseases is still high due to large-scale poverty, inadequate health policies and government policies [Aparajita & Ramanakumar 2005]. Global health agencies and policy-makers play essential role at national and sub-national level for designing adequate public-health policies [Walker et al., 2007].

Unfortunately, COVID-19 has already affected 6 million worldwide causing 12% death of the affected population. In India, with 73 million people living in poverty and improper sanitation conditions, new healthcare policies should be designed by considering problems of Rural India as well. The health services should be re-distributed creating a link between families, communities, government, and corporations[Aparajita & Ramanakumar 2005]. With only 1.28% of GDP contributions of India for health, a very comprehensive health care policy is needed, where private sector should come forward and partner with government facilities to address the COVID-19 situation in the country. Equalization in terms of treatment and patient care throughout the country for coping up with COVID-19 should be considered.

Alternative Measures under 'Herd Immunity'

COVID-19 will continue to exist until immunity against it is acquired through natural (sufficient infection of world's population) or acquired (vaccine) ways [Brodin, 2020]. Critical analysis of measures to control or treat COVID-19 by closing school, universities, followed by completely locking down cities or countries, is taking us to an alternative strategy of Herd Immunity. Alternate strategy suggested by Kwok et al.,2020 was to expose the population apart from elderly and people with co-morbidities to SARS-CoV-2 in order to increase population immunity. Antibody Cross- Reactivity and Partial immunity

(or other common coronaviruses) may contribute towards achieving herd immunity. However, by the time herd immunity is acquired, the number of people who could potentially die of COVID-19 will be too adverse to accept [Kwok et al., 2020]. Yet another strategy, while approaching towards herd immunity, that can be applied is where the patients recovered from COVID-19 can be temporarily employed at the hospital settings based on their skill set. But in such indirect immunity approach, we are still lacking results on 're-infection'. Also herd immunity will prove ineffective if the virus mutates, and this possibility cannot be ruled out completely [Ryan et al., 2020].

United Kingdom's plan to save lives was pivoted around herd immunity. However, when brutal consequences were observed, the strategy was ruled impermissible [Horton., 2020]. Thus, lockdown might effectively delay the rate at which India will acquire herd immunity as abrupt exposure to 1.2 billion population to the virus will put stress on the health care sector. However, early June, India lifted lockdown and eased restrictions on mobility of people. Therefore, crucial strategies need to be set, like, additional research on mutated strains of SARS-CoV-2, reports on re-infection, proper age-related survey of COVID-19 infection, setting up of primary care unit in COVID-19 hotspots and idea of corporation, government and political sector working together. Proper implementation of these strategies will ultimately help India combat this pandemic. Thus, policy makers should strategize economic revival depending upon the best possible data and critical understanding [Altmann et al., 2020].

Conclusion:

The current review article focuses on the control, epidemiology, diagnosis, possible treatment, economic, social and educational impact of SARS-CoV-19 infection. The availability of various treatment options and their shortcomings (if any) suggests that heavy clinical trials should be conducted world-wide to check the efficacy and safety of the anti-viral therapy or immunotherapy or both as an option to successfully treating COVID-19 with maximum positive outcomes. Isolating patients, social distancing and Lockdown although will cause damage to the economy of the nations, remain the key aspects to manage COVID-19 spread in heavily affected countries including India. There is a need for expanding the healthcare workforce, synthesizing quick and effective diagnostic tools and mass testing to manage COVID-19 effectively. The dire outbreak of COVID-19 has shined light onto many sectors that require immediate attention for improvement. The revival of a country from COVID-19 outbreak will not only depend on the fiscal stimulus adopted by the policy makers but will also be determined by the cooperation and responsible behavior regarding personal sanitation embraced by its citizens.

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