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"Let food be thy medicine"- Could Indian Diet Contributed to the Survival Rate of COVID-19 patients in India?

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ABSTRACT
Coronavirus disease (COVID-19) is an infectious disease caused by coronavirus. Many people infected with the COVID-19 virus experienced mild to moderate respiratory illness and recover without requiring special treatment. However, the intensity of infection varied from country to country. The mortality rates in affluent countries with better health care were much higher than the less affluent countries with limited health care system. The death rate in Southeast Asia was low and the mortality in India was low according to the publications. This paper tries to present a review the disease and probable reasons for low mortality in India.

KEY WORDS: covid-19, prophylactic, treatment, aspirin, salicylates, Indian diet, Low mortality.

I. INTRODUCTION

In late December 2019, a virus emerged from Wuhan, China which resulted in a formidable outbreak in China and expanded globally, affecting millions of people. [1, 2] The International Committee on Taxonomy of Viruses (ICTV) named the new virus "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)" as Coronavirus Disease-2019 (COVID-19 on 11 February 2020. [3] The virus is the third zoonotic coronavirus, after SARS-CoV and MERS-CoV, but with pandemic potential. [2] they predicted it to cause low to moderate (estimated 2%–5%) mortality rate. [1] Today the world is in a pandemic caused by the virus and resulted in severe acute respiratory syndrome which causes serious respiratory tract infections that lead to pneumonia, acute respiratory distress syndrome and even death.[4]

The disease spreads from Person-to-person through droplet and contact. Hence they suggested social distancing, wearing masks and frequent washing of hands for reducing or preventing the disease transmission. The authorities in almost all countries implemented lockdown to prevent the spread of disease. They provided first line health workers with Personal Protective Equipment (PPE) for stringent infection control.

The discussion on virology, epidemiology, clinical manifestations, diagnosis and prevention is elsewhere.[1] There is no standard treatment for the disease, and supportive treatment was the only strategy. [5]. Early screening of critically ill patients and critical care-guided early intervention helped in reducing COVID-19 patients' mortality.[6] Various known drugs can reduce the severity of the disease.[7] Many countries are working to develop a vaccine and India has launched a vaccination programme with vaccine it has developed.[8]

The symptoms of COVID-19 patients

The symptoms of COVID-19 patients differed from person to person and depended on the severity of the infection.[9] However, "fever and cough are the most prevalent symptoms of adults infected by SARS-CoV-2.affected with COVID-19". [10] Respiratory complications were common, but non-respiratory complications were also observed.[9] Studies showed that SARS-CoV-2 infection causes multisystem disease and significant pathology in most organs in patients with and without comorbidities.[11]

Resolving the mystery of death during COVID-19 pandemic

The primary reasons for death among the virus-infected patients is not very conclusive because in many records they documented it as 'Dying due to' and 'Dying with' COVID-19, which made situation very complex. However, with the limited data available, we can draw some conclusions to identify the most probable causes for death among virus-infected patients.[11,12]. In most persons died after testing positive for SARS-CoV-2, the cause of death was COVID-19. In a large proportion of death certificates, they reported no comorbidities, suggesting that this condition can also be fatal in healthy persons. [13]

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Autopsy reports give an insight into the prime cause of disease.

Findings of 15 forensic autopsies performed in Romania records the most frequent symptoms before death were dry cough, dyspnoea, and fever. Hypertension, ischemic cardiac disease, and a history of stroke were the most frequent associated diseases. "The mean duration from the symptoms' debut to a RT-PCR positive SARS-CoV-2 test was 3.7 days, while the mean survival time from the RT-PCR positive test was 4.2 days".[14] The histological examination in seven cases revealed hyaline membranes, and mixed inflammatory cell infiltration of the interstitium, alveoli, and perivascular areas. In addition, all the examined cases developed "small vessel thrombosis".[14]

Studies on series of 68 autopsies from Italy and New York City showed a consistent pattern of tracheobronchitis, alveolar injury, and vascular/thrombotic disease in patients with frequent co-morbidities such as hypertension and diabetes. However, an important observation was the high frequency of thrombi, especially platelet thrombi. [15]

The above observations led to a cohort study of pulmonary embolism (PE) observed in autopsies conducted from January 2017-April 2020, and they reported increased risk of PE related to COVID-19.[16]`Venous thromboembolism was more common than arterial thromboembolism in hospitalized COVID-19 patients. They observed pulmonary thrombosis and microvascular thrombosis in their studies and concluded that "Microvascular and macrovascular thrombi suggest hemostatic imbalances may contribute to the pathophysiology of SARS-CoV-2 infection"[16] Thus coagulation abnormalities and thrombosis was one characteristic of the infection. [17] Another study showed megakaryocytes and platelet-fibrin thrombi in multi-organ thrombosis in the autopsies of COVID-19 patients.]18] We discuss elsewhere hypothesis on the mechanism of thrombotic formation. [19]

Coagulopathy- the common defect among COVID-19 patients

"The onset of coagulopathy in COVID-19 patients is one of the most important signs of poor prognosis". [20] Corroboration of clinical findings with biochemical studies reported that "multiple systems contribute to thrombosis in COVID-19 patients, such as activation of coagulation, platelet activation, hypo fibrinolysis, endothelial cell dysfunction, inflammation, neutrophil extracellular traps, and complement".[17] Marked D-dimer elevation is a predictor of mortality and hence hospitalisation is recommended for patients with high D-dimer levels.{21] [22]. One study concluded that D-dimer, Pro-calcitonin (PCT), and Lactic dehydrogenase (LDH) were superior to serum ferritin and C-reactive protein (CRP) as an effective biomarker in predicting the fatality of COVID-19.[23] D-dimer on admission greater than 2.0 µg/mL (fourfold increase) could effectively predict in-hospital mortality in patients with COVID-19, which showed D-dimer could be an early and helpful marker to improve management of COVID-19 patients, according to Chinese Clinical Trial Registry: ChiCTR2000031428.[21] coagulopathy was present in up to 50% of patients with severe COVID-19. [24] Therefore hypercoagulability may be a mechanism that contributes to the adverse outcomes of COVID-19.[25,26]

Treatment for hypercoagulability -Targeting thrombosis and improving lung function

The attention of researchers turned to target different pathways to reduce thrombosis and improve lung function in COVID-19 patients. One immediate method was to suggest moderate exercises. Exercise mitigates many of the identified side effects from the pharmaceutical agents being trialled. Therefore, low- to moderate-intensity exercise could be an adjuvant therapy for people with mild-to-moderate COVID-19 and may reduce the risk of developing severe symptoms of illness.[27]

Use of anticoagulants in COVID patients

Another method is to use anticoagulants. They have reported improved prognosis in the COVID-19 patients associated with hypercoagulability on administration of anticoagulants [28] and "therapeutic anticoagulation is considered as the cornerstone to treat thrombosis and PE".[29] They suggested the rationale for using heparin.[30} "There are several ways in which probably heparin administration can benefit patients with COVID-19, beyond the anticoagulant effect."[31] It created debate within the critical care community on the therapeutic utility of heparin. The International Society on Thrombosis and Haemostasis (ISTH) and the American Society of Hematology (ASH) have recommended prophylactic LMWH, but the best effective dosage is uncertain.[29]

Using Acetylsalicylic Acid (ASA) for adult patients with COVID-19 was suggested.[32] Recently, the study on aspirin as an anticoagulant reported a lower "mechanical ventilation, intensive care unit (ICU) Admission, and In-Hospital

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mortality in hospitalized patients with COVID-19".[33] According to them "the patients given aspirin were 43% less likely to be admitted to the ICU, 44% less likely to be placed on mechanical ventilation, and 47% less likely to die in the hospital.[33]

Thus the recent studies point to the effectiveness of anticoagulants, like heparin and aspirin in treating COVID-19 patients.

Low mortality of COVID-19 patients in India

The pattern of infection and mortality rates of COVID-19 patients from various countries shows a low mortality in Southeast Asian countries, especially in India. Mortality rate in affluent countries with greater healthcare was higher than less affluent countries.[34]. The authors have discussed the probable reasons.

India's report on low mortality because of COVID-19 was contested and we reproduce their comments below.

"India has had 3·6 million cases of COVID-19, the third most in the world after the USA and Brazil, with 65 288 officially confirmed deaths from the disease as of Sept 1, 2020.

The Indian Government says that the national recovery rate has reached 77% and the case fatality rate is down to 1·8%, due to "timely and effective clinical management of the patients in critical care" according to an official statement on Aug 30. However, experts who spoke with *The Lancet* have pointed to several sources of uncertainty in India's COVID-19 mortality data". [35]

Against such a backdrop, this paper attempts to explain the reasons for low mortality in India and tries to close the gap.

There are three reasons for the low mortality. We start with minor reasons first.

1) Early detection and treatment by lay persons

Boisar (Tarapur) is an industrialised area close to Mumbai in Maharashtra. The Covid Care Centre, near Betagoan was almost full with COVID-19 patients. They transferred patients to the centre, accompanied by health workers and police. People wanted to escape the stigma associated with COVID-19 infection. The industries did not want to lose workforce, and they guided the employees for treatment. They did not wait for the RT-PCR results. So many people took medication and did self quarantine in their apartments. They all recovered from the infection because they started treatment at the onset of probable symptoms. We hardly heard any deaths in this town. They transferred a few seriously ill patients to Mumbai for better treatment, and they survived.

2) Severity and transmission of COVID-19 depends on the initial dose of inoculum

An important observation made was many members of the family staying with COVID-19 patients in the same apartments did not get any infection. It may be due to open ventilated homes in India, which reduces the viral load in the air.

India being a tropical humid country has an open ventilation system at homes, workplaces and hospitals. Modern architecture of buildings uses certain traditional designs. The traditional house design in Kerala is a courtyard house or *Nalukettu* and it is four blocks built around an open space in the centre. Hot air from the central courtyard rises to the top due to wind blowing above the house and creates a draft upwards following Bernoulli's principle of fluid dynamics. The air from outside enters the house through perforations and windows and replaces the rising hot air from the open courtyard. [36]Thus there is a continuous air flow from outside into the house, moving upwards through the central courtyard. In modern multi-storeyed buildings in Mumbai, the windows of washrooms of all the flats in the same floor connect to the central conduit opening to the sky, helping to reduce foul smells from the washroom by passive air draft which may reduce viral load in the flats.

Severity and transmission dynamics of COVID-19 depend on the viral dose [37,38] which dep[ends on the ventilation. The houses and working environment In affluent countries have a closed ventilator system. The houses and working environment in India have an open ventilation system which contribute to low viral load in the houses and working environment. Low viral load yields low inoculum and reduces the severity of disease. This may have contributed to the higher recovery rate of COVID-19 patients in India.

3) Salicylates in Indian foods

Recent studies direct researchers to anticoagulants like heparin and aspirin. Aspirin is acetylsalicylic acid, and they originally extracted it from willow bark. Aspirin has antiviral properties [39]. The results of on-going clinical trials reports "the early use of aspirin in covid-19 patients, which has the effects of inhibiting virus replication, anti-platelet aggregation, anti-inflammatory and anti-lung injury, is expected to reduce the incidence of severe and critical patients, shorten the length of hospital duration and reduce the incidence of cardiovascular complications". [40]

Plants produce "Salicylic acid and related compounds as part of their defence systems against pathogen attack and environmental stress".[41] Its history, metabolism and disease we discuss elsewhere preventing properties [41]. We discuss elsewhere salicylates content in various foods and its implications. [42,43]

The Western diet is meat and dairy products which are very low in salicylates while Indian diets are rich in salicylates.[44] Even the diet of poorest of poor in India comprising rice or roti with chilli powder and salt or vada pav with cayenne pepper may have adequate salicylates. Indian spices and garam masala are a rich source of salicylates. [44,45]

Salicylates improves blood flow and has an advantage in certain health conditions and also the recovery and repair of certain injuries. Curry powder, Cayenne pepper, Ginger, Cinnamon, Turmeric, Garlic, Onions Vitamin D are rich in salicylates. [47,48]. Therefore, we can conclude that salicylates in the Indian diet may have acted like aspirin in the covid patients and it may have contributed to the survival rate of COVID-19 patients in India.

The author likes to conclude this paper on a lighter note and tweak a dialogue in Chennai Express (2013) movie, "Do not underestimate the power of Indian Diet".

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