Clinical Insights into SARS-COV-2 Infection in Rural Rajasthan, India

Anand Derashri¹, Shivadatta Padhi², Dinesh Vaishnav³, Anish Jain⁴, Ruma Bose⁵, Vandana Tyagi⁶

¹Junior Consultant, Anaesthesia Shri Sanwaliyaji District Government Hospital, Chittorgarh, Rajasthan India, ²Consultant Gastroenterologist, Medishine Hospital, Raipur Chattisgarh, India; Ex-senior Resident Gastroenterology, Sawai Man Singh Medical College, Jaipur, India, ³Consultant Surgeon, Shri Sanwaliyaji Government Hospital District, Chitorgarh, Rajasthan, India, ⁴Consultant Internal Medicine, Shri Sanwaliyaji Government Hospital District, Chittorgarh, Rajasthan, India, ⁵Department of Anaesthesiology, Critical Care and Pain Medicine, Beth Israel Deaconess Medical Centre, Assistant Professor, Harvard Medical School, Boston, MA, ⁶Ex-attending Consultant, Department of Critical Care, Fortis Hospital, Mulund Mumbai, India; Ex-Senior Clinical fellow (Critical Care) Royal Brompton and Harefield NHS Trust UK, Ex-junior consultant, Critical Care Services Specialty, Medical ICU, SMS Hospital, Jaipur, Rajasthan, India

Abstract

Background: This study aimed to highlight the primary endpoint of death and to understand the clinical and epidemiological characteristics of COVID-19 infection in the rural community of Chittorgarh, Rajasthan, India.

Method: This was a retrospective, observational study of COVID-19 patients from March to June 2020 that collected and analysed epidemiological, clinical, laboratory, and radiological data.

Results: In 353 patients, COVID-19 affected all age groups, mainly those aged 16–49 years, followed by those aged 50–64 years; 82.43% were male; 68% of infected patients were asymptomatic at presentation and were incidentally positive on contact tracing. Among symptomatic cases, fever (88%) was the most common symptom; of 14 severe COVID-19 patients with pneumonia, 8 died. Leukopenia, lymphopenia, thrombocytopenia, and abnormal liver function tests were common lab findings. Thirty patients had radiographic evidence of pneumonia. The most common complications were acute respiratory distress syndrome, multiple organ dysfunction syndrome, and kidney injury. The case fatality rate was 0.02%, and the Sequential Organ Failure Assessment score>6 was a surrogate marker for admittance to the intensive care unit.

Conclusion: Low case fatality rate and SOFA score surrogate for ICU admittance.

Keywords: SARS-CoV-2, novel coronavirus pneumonia, rural community, severity, SOFA score.

Introduction

Coronavirus disease 2019 (COVID-19) is caused by coronavirus-2 (SARS-CoV-2) and may lead to severe acute respiratory syndrome; SARS-CoV-2 is an enveloped, single-stranded, positive-sense RNA virus that varies in length from 26–32 kb. COVID-19 originated in Wuhan, China in December 2019, and the World Health Organization (WHO) declared it a pandemic on 11 March 2020. Phylogenetic analysis has revealed four viral clades: O (ancestral clade from China), B (from China), A3 (from Iran), and A2a (from
Iran, Europe, and other countries); these clades are in circulation in India, with A2a comprising the dominant type.\textsuperscript{2}

Since the first laboratory-confirmed case of SARS-CoV-2 in India was reported in Kerala on 30 January 2020, patients with COVID-19 pneumonia have been presenting to hospital emergency departments with severe acute respiratory illness (SARI).\textsuperscript{3}

The transmission of SARS-CoV-2 is usually via airborne droplets to nasal mucosa in closed environments, by close contact between people, and by touching contaminated surfaces; the incubation period is 2–14 days with a basic reproduction number of 2.2.\textsuperscript{4}

The COVID-19 infection spectrum consists of asymptomatic infection, mild upper respiratory tract illness, fever, cough, shortness of breath, pneumonia, and other respiratory tract symptoms. In many cases, these symptoms progress to severe respiratory failure and death.\textsuperscript{4}

In India, the initial COVID-19 testing strategy included people who had an international travel history with symptoms, symptomatic contacts of lab-confirmed COVID-19 patients, and symptomatic health care workers managing patients with influenza-like illness or SARI. The case definition for influenza-like illness was a fever of >38°C, cough, and onset within the last 10 days. The SARI case definition was an acute respiratory infection with a history of or current fever >38°C, cough, and onset within the last 10 days that required hospitalisation.

Suspected cases and positive cases based on reverse transcriptase-polymerase chain reaction (RT-PCR) results were initially admitted in a separate, designated isolation area at Shri Sanwaliyaji Government District Hospital Chittorgarh starting 23 May 23 until 8 May 2020, from then onwards consistent with the dynamic health situation, the Rajasthan government established COVID-19 care facilities at Shri Sanwaliyaji Government District Hospital Chittorgarh on 8 May 2020 for mild and moderate illness, with five satellite quarantine care facilities operated concurrently; patients with severe illness were referred to the Rabindra Nath Tagore Medical College and COVID Centre, Maharana Bhupal Government Hospital Udaipur, for special and critical care facilities after initial stabilisation at our centre. The COVID care centre placed separately had 100 beds with 56 (high-dependency unit [HDU] = 6, intensive care unit [ICU] = 4) additional 120 beds in main hospital (HDU = 48, ICU = 15). Apart from medical treatment, a nutritious diet, psychological counselling, and nursing care were provided, and patients with mild to moderate disease were provided yoga therapy. This study was carried out to document the community based clinical and epidemiological characteristics of SARS-CoV-2 infection in rural Rajasthan making it distinct from urban and hospital based studies.

The testing strategy adopted was according to Indian Council of Medical Research (ICMR) guidelines. The purpose of the current study was to analyse and describe the epidemiological and clinical characteristics of COVID-19-positive SARI cases during a 4-month period from 23 March to 23 July 2020.

**Method**

This retrospective, observational study included adult patients with SARI admitted to the COVID care facility in Chittorgarh, the designated management centre for mild and moderate illness that included a quarantine care facility. Necessary preventive measures and management protocols for all patients with suspected infection, as suggested by the Indian Ministry of Health and Family Welfare, were followed. The study was cleared by the ethical committee of the hospital.

All patients were triaged for SARI in a separate isolation area, and all infection prevention and control practices were followed, including personal protective gear for the physicians, nurses, and paramedical staff as per the protocol of the Ministry of Health and Family Welfare. The isolation facility at the COVID care centre was assessed for preparedness according to a standardised checklist from the National Centre for Disease Control in New Delhi.

**Data Collection:** Epidemiological, demographic, laboratory, clinical management, and outcome data were extracted from the database of all patients with SARI admitted to the centre. The data were checked by three independent physicians; a fourth researcher adjudicated any difference in interpretation.

**Study Outcomes:** The primary composite endpoint was ICU admission, use of mechanical ventilation, or death.

**Laboratory Procedures:** Nasal or oropharyngeal swabs were obtained from all patients with SARI depending on patient cooperation and were tested for
confirmation of SARS-CoV-2 using real-time RT-PCR (rRT-PCR). Specimens were obtained on day 1 of admission and again on day 5 if the first sample was negative. After collection, the nasal and pharyngeal swabs were inserted into the same 2-mL cryovial containing viral transport medium. The swabs were pressed to the side of the cryovials and then broken off into the cryovials. Specimens were stored and transported to the laboratory at 4°C. A single positive test was sufficient to declare positive results. For patients with SARI who exhibited a highly suspicious radiological appearance on chest radiographs, two consecutive negative tests were conducted before being discharged or transferred to the non-COVID area at the facility.

Routine blood examinations included complete blood count, arterial blood gases, coagulation profile, and serum biochemical tests for renal and liver function, creatinine kinase, lactate dehydrogenase, electrolytes, and cardiac enzymes. Chest radiographs were performed for all patients. The frequency of examinations was determined by the treating physician. All epidemiological, clinical, and laboratory data were recorded.

**Definitions:** Fever was defined as an axillary temperature ≥37.5°C. Sepsis and septic shock were defined according to the 2016 Third International Consensus Definition for Sepsis and Septic Shock. Acute kidney injury (AKI) was diagnosed according to Kidney Disease: Improving Global Outcomes clinical practice guidelines. Acute respiratory distress syndrome (ARDS) was diagnosed as per the Berlin definition.

Secondary infection was diagnosed when patient developed signs and symptoms of pneumonia or bacteraemia and a positive culture of a new pathogen was obtained from lower respiratory tract specimens (qualified sputum, endotracheal aspirate, or bronchoalveolar lavage fluid) or blood samples after admission.

Acute cardiac injury was diagnosed if serum levels of the cardiac biomarker creatine kinase (CK)-MB was above 99th percentile of the upper reference limit or if new abnormalities were detected on electrocardiography or echocardiography. Myocarditis was diagnosed based on acute chest pain suggestive of cardiac origin, acute onset of tachycardia or bradycardia on electrocardiography, intraventricular conduction defects, and secondary ST-T wave changes.

Hypoaalbuminemia was diagnosed as serum albumin <3.5 g/L. Leucopenia was defined as absolute leucocyte count <4000/mm³. Lymphocytopenia was defined as absolute lymphocyte count <1500/mm³. Thrombocytopenia was defined as platelet count <150,000/mm³. Monocytosis was defined as absolute monocyte count >950/mm³.

As per WHO guidelines, COVID-19 pneumonia was considered as severe if the patient had fever or suspected respiratory infection plus one of the following: 1) respiratory rate >30 breaths per minute, 2) severe respiratory distress, or 3) SpO₂ ≤93%. Patients with COVID-19 pneumonia not fulfilling the criteria for severe pneumonia were considered to have non-severe COVID-19 pneumonia.

**Results**

Patient characteristics are reported in Table 1. There were 353 COVID-19-infected individuals, of whom 291 (82.43%) were male. The predominant age group at presentation was 16–49 years, followed by 50–64 years. Two hundred forty (68%) infected patients were asymptomatic at presentation and were determined to be positive upon active community contact tracing by public health officials. Fourteen had COVID-19 infection and were initially managed at the COVID care centre but were subsequently referred to the dedicated centre for severe COVID-19 patients at Rabindra Nath Tagore Medical College Udaipur.

In individuals who were symptomatic at presentation, the median duration from onset of symptoms to admission in the COVID care centre was 3 days. These patients included 4 health care professionals, 3 municipality staff, 2 police force members, and 8 prisoners all of these recovered.

Among symptomatic cases, fever (88%) was the most common symptom at presentation followed by sore throat (85%), body aches (72%), anosmia (1%), altered taste sensation (1%), dyspnoea, rhinorrhea (<1%), diarrhoea, and abdominal pain (<1%). One young patient initially presented with myocardial infarction; no patients presented with stroke or deep venous thrombosis. Two patients, one in puerperium and another in the first trimester of pregnancy, were positive and had an uneventful recovery.

There were 14 severe COVID-19 pneumonia cases referred to the COVID care centre for further treatment:
8 of these patients died, 5 of whom had 1 or more comorbidities; the remaining 6 patients were transferred to the community COVID care facility upon stabilisation.

Thirty-nine subjects had a history of underlying chronic obstructive pulmonary disease and were predominantly male, 11 had type 2 diabetes mellitus, 17 had hypertension, 2 had an underlying malignancy, and 2 had underlying chronic kidney disease. Three patients had silent hypoxia at presentation.

Radiological and laboratory findings: The laboratory parameters and clinical characteristics of patients with COVID-19 are shown in Tables 2, 3, and 4. Thirty patients exhibited radiographic features suggestive of pneumonia. The most common pattern on chest radiograph was bilateral patchy nodular or interstitial shadows in 26 patients; other patterns included peripheral interstitial infiltrates and basal nodular interstitial infiltrates. Two patients had unilateral infiltrates. No patients had pneumothorax or pneumomediastinum.

Leucopenia was observed in 32 patients, thrombocytopenia in 9; and lymphopenia in 2; no patients displayed monocytosis. Hypoalbuminemia was present in 4 of the 14 patients with severe COVID-19 pneumonia; no other patients had hypoalbuminemia. An elevated CK-MB level was observed in 2 patients and AKI was in 8 patients with severe COVID-19 pneumonia. Accordingly, hypoalbuminemia and AKI were observed in patients with severe COVID pneumonia who one of the primary outcomes.

Vital signs and organ dysfunction: Vital signs and clinical characteristics are reported in Table 4. Patients with severe COVID-19 pneumonia more frequently exhibited tachycardia, tachypnoea, and reduced SpO₂ (<93%) and PaO₂. These patients also had one or more organ injury in the form of AKI and elevated CK-MB level and SOFA scores.

Of the 14 patients with severe COVID-19, 10 were male and 4 were female, 8 had comorbidities, and 6 had no comorbidities. Five of 8 patients who died had comorbidities, of which chronic obstructive pulmonary disease (COPD) was the most common, followed by diabetes, hypertension, and obesity; the age range of those who died was 50–80 years; 5 were male, and 3 were female. Among the 8 who died, 1 had single organ dysfunction, and 7 had multi-organ dysfunction.

Treatment and main interventions: All patients with SARI received oral antibiotics (oseltamivir 75-mg tablets twice daily for 5 days, azithromycin 500-mg tablets once daily for 5 days); those with SpO₂<92% received supplemental oxygen therapy. Patients who tested positive were given hydroxychloroquine (400 twice daily on day 1 followed by 200 mg twice daily for 4 days) and azithromycin (500 mg once daily). Those with a low bleeding score were given low-molecular weight heparin on a case-to-case basis. Ten patients received vasopressors. Thirty-three patients required oxygen, including 14 who required ICU care, 12 of whom required mechanical ventilation.

### Table No: 1: Characteristics of study population

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Patients n=353</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M</td>
<td>F</td>
</tr>
<tr>
<td>Age (in years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>16-49</td>
<td>235</td>
<td>46</td>
</tr>
<tr>
<td>50-64</td>
<td>45</td>
<td>13</td>
</tr>
<tr>
<td>&gt;65</td>
<td>9</td>
<td>3</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>291</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>62</td>
<td></td>
</tr>
<tr>
<td>Residence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rural/semi urban</td>
<td>353</td>
<td>100%</td>
</tr>
</tbody>
</table>
### Table No. 2: Clinical profile of COVID-19 infected individuals

<table>
<thead>
<tr>
<th>Profession</th>
<th>Patients n=353</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Health Workers</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Sanitation workers/Civic Administration including police</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Others (agricultural workers/businessmen, other population)</td>
<td>340</td>
<td></td>
</tr>
<tr>
<td>H/O travel to infected region H/O contact with laboratory confirmed case</td>
<td>40</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table No. 3: Laboratory and radiological features of COVID-19 subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Investigation</td>
</tr>
<tr>
<td>White blood cell count</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Absolute lymphocyte count</td>
</tr>
<tr>
<td>Platelet count</td>
</tr>
<tr>
<td>Srcreatinine</td>
</tr>
<tr>
<td>Total Bilirubin</td>
</tr>
<tr>
<td>Alkaline phosphatase</td>
</tr>
<tr>
<td>AST</td>
</tr>
<tr>
<td>ALT</td>
</tr>
</tbody>
</table>
Investigation                        | Value                | Subjects (n=353) |
-----------------------------------|----------------------|-----------------|
SrCRP >3mg/L                       |                      | 16              |
ESR >20mm/hr                       |                      | 56              |
SrLDH >234U/L                      |                      | 45              |
Raised CKMB                         |                      | 9               |
Raised Trop(I)                     |                      | 1               |
Atypical pneumonia in chest xray   |                      | 30              |

Table No. 4: Outcomes in relation to co-morbidities in severe COVID-19 cases

<table>
<thead>
<tr>
<th>Number of patients n=14</th>
<th>Incidence of death n=8</th>
<th>Incidence of discharge n=6</th>
</tr>
</thead>
<tbody>
<tr>
<td>With Comorbidities</td>
<td>Without Comorbidities</td>
<td>With Comorbidities</td>
</tr>
<tr>
<td>8</td>
<td>6</td>
<td>5</td>
</tr>
</tbody>
</table>

Table No. 5: Outcomes in relation to SOFA score

<table>
<thead>
<tr>
<th>Number of patients</th>
<th>Incidence of death</th>
<th>Incidence of discharge</th>
</tr>
</thead>
<tbody>
<tr>
<td>SOFA score</td>
<td>SOFA score</td>
<td>SOFA score</td>
</tr>
<tr>
<td>0-8</td>
<td>9-16</td>
<td>17-24</td>
</tr>
<tr>
<td>4</td>
<td>2</td>
<td>8</td>
</tr>
</tbody>
</table>

Discussion

The progression of the COVID-19 pandemic in India can be divided into three frames of progression as follows.

The initial period of early lock down by government of India starting from March 25, 2020: During this time, cases were predominantly individuals living in urban areas, those returning from COVID-19-affected countries and predominantly affected urban areas and their contacts, including tourists.

The period starting from the migrant labour movement, somewhere in the midst of the lockdown until the guarded unlocking: During this time, cases started to rise in semi-urban and rural areas due to migrant labourers.

The period of guarded unlocking from 1 June 2020 until the date with constraints on the unlocking in containment zones. During this time, cases continued to rise in rural and semi-urban areas as the process of guarded unlocking was undertaken.

The present study represents one of the largest cohorts of a semi-urban and rural population for a COVID-19 study and is community-based, as the COVID care centre was the first point of contact in the community in association with the COVID health care facility; hence, the patients are representative of the rural population of southern Rajasthan, India. Accordingly, these data represent the community-based epidemiological and clinical pattern of COVID-19 in this rural population, which is distinct from the hospital-based data from urban centres that display different socioeconomic and demographic characteristics; the hospital-based data representing a semi-urban and rural population may represent more serious and critical patients and thus differ in their findings.

At our centre, 353 COVID-19-infected individuals were observed and treated. The median time from symptom onset to COVID care centre admission was 3 days, which included the delay in logistical arrangements and sample processing. COVID-19 affected all ages ranging 5–80 years. Most were aged 16–49 years (59.49%), followed by 50–64 years (16.43%). Male patients constituted the majority, as younger men are more likely to be mobile and hence more susceptible to infection. This finding is consistent with other studies reporting a similar male preponderance.4,5
The clinical spectrum of COVID-19 varies widely from asymptomatic to critical illness. In the present series, most infected patients were asymptomatic (68%), which contradicts the findings of Gupta et al, who reported that 42.9% of patients were asymptomatic. Asymptomatic subjects may recover without experiencing symptoms. More recently, the proportion of infected of mild or asymptomatic cases was estimated to comprise 60% of all infections; this is comparable to the present finding of 68%. Symptomatic and asymptomatic patients exhibit a comparable viral load, suggesting a strong transmission potential; hence, this is of important public health significance in controlling spread of COVID-19.

Ideally, large-scale screening using antibody testing should be combined with rT-PCR; however, in our study, only rT-PCR testing of nasopharyngeal swabs was performed as per the prevalent guidelines by the regional health agency.

Among 113 symptomatic patients, the most common symptoms were fever (78%), sore throat and cough (76%), and body aches and myalgia (64%). Less common symptoms included headache, abdominal pain, nasal discharge, chest pain, anosmia, vomiting, and chemosensory dysfunction. Atypical symptoms such as loose stool, altered sensorium, and painful abdomen were found in <1% of patients. Some hospital-based studies have reported dyspnoea as the most common symptom at hospital admission; however, our study showed sore throat, malaise, and body aches as the most common symptoms—this may be due to the community representation comprising our database. Most studies have reported gastrointestinal symptoms including nausea, vomiting, and diarrhoea, with an incidence of less than 10%. In addition, Bhandari et al observed that cough was a major symptom, followed by fever, whereas Wang et al reported fever as the most common symptom.

Of the 353 infected patients, 57 (16.1%) had comorbidities, of which COPD was the most common (39 [68.42]), followed by hypertension (17 [29.82%]), diabetes mellitus (11 [19.2%]), cardiovascular disease (2 [3.5%]), chronic kidney disease (2 [3.5%]), and malignancy (2 [3.5 %]). Patients with severe COVID-19 infection had one or more comorbidities. The most common coexisting illness in patients who met one of the primary outcome was COPD, followed by diabetes and hypertension; these patients were also more likely to be have one or more underlying comorbidities.

In relation to complete blood cell counts, leucopenia was present in 20.96% of patients, lymphocytopenia in 4.8%, monocytecytosis in <1%, and thrombocytopenia in 25.49%. In similar studies, Bhandari et al and Zhang et al reported higher incidences of lymphopenia at 52.3% and 75.4%, respectively; this can likely be explained by the predominance of asymptomatic patients in the present study. In addition, serum creatinine was elevated in 16 patients (4.5%) and abnormal liver function tests were observed in 24 patients (67.98%), with elevated aspartate transferase in 65.1% and elevated alanine aminotransferase in 50.9%. Followed by elevated levels of alanine aminotransferase, aspartate aminotransferase, and bilirubin. Viral infections are often associated with “bystander hepatitis”, indicating mild elevations of transaminases without compromised liver function. This may also be observed with COVID-19 infection for which liver failure has not been reported, even in the most severe and fatal cases.

AKI was observed in 16 patients and in all who met one of the primary outcome. Three postulated mechanisms include a direct viral effect on nephrons, sustained hypoxia due to type I respiratory failure, and circulatory shock. Moreover, elevated CK-MB was significantly increased in 2 patients who died, but it was not correlated with troponin-I levels or electrocardiographic changes; this may be because CK-MB is more commonly associated with thrombo-inflammation rather than a cardiac origin.

Guau et al reported that patients with comorbidities had a 1.79–2.59 times greater risk of mortality when compared to patients without comorbidities. Similarly, in a meta-analysis, Yang et al stated that the odds ratio of developing severe disease in patients with hypertension, respiratory disease, or cardiovascular disease was 2.36–3.42.

In contrast to prior results, the relative risk of death in patients with comorbidities in our series was 1.7. This may be because we studied a rural, community-based cohort, rather than a hospital-based cohort; moreover, in the prior studies, the authors defined their endpoints as invasive ventilation, severe disease, and death, further more the, populations of these studies were genetically, immunologically and geographically distinct from the study population.

Furthermore, high mean SOFA scores (Table 7) are a red-flag sign and a surrogate marker for initiation of
early intensive care therapy, and Vincent et al previously stressed the role of organ failure on mortality in patients with COVID-19. In our series, relative risk of death in patients with multi-organ dysfunction was higher than that compared to patients with single-organ dysfunction; moreover, the relative risk of patients with COVID-19 and a SOFA score ≥17 was more than twice that of patients ≤16; these findings are similar to those of Ruan et al.17

The case fatality rate in our study was 0.02. Each country and its various regions have unique advantages and problems while dealing and reporting in a pandemic; when analysed, this will provide data that can be used for more effective management of the COVID-19 pandemic. Contact tracing, early timely lockdown measures, and guarded unlocking with use of circuit breaker lockdowns as cases spiked during guarded unlocking were actively undertaken by health authorities in Rajasthan; this led to early infection identification, partially mitigating complications because of delayed diagnosis. This may also contribute in part to the abundance of mild and moderate cases and fewer complicated severe cases in the study cohort, although there are other possible explanations such as rural demographics and population distribution, less overcrowding, and a relatively large young population. The COVID-19 fatality rate in India is among the lowest in the world (2.8% against a global average of 4.7%), and the disease has also been observed to be less severe among Indians, with a significantly higher recovery rate (60.9% versus a global average of 56.6%) and doubling time (20.3 days) as compared to populations elsewhere.18-20

Intriguingly, case fatality rates in India as a whole are lower than that in Western countries. There are several postulated causes that may explain this phenomenon. First, Indians are exposed to a relatively abundant microbial load early in life, conferring broad-based immunity to the population.21,22 Second, immunological variations result from heritable and non-heritable influences. Heritable factors include germline inheritance, which exhibits only a minor influence on inter-individual and population variation in immune responses.23,24 Heritable factors account for only 22% of the overall variation in gene expression.25 In contrast, non-heritable influences are the major factor driving immunological variation and include environmental influences, such as infections, vaccines, stochastic epigenetic changes arising from imperfect replication machinery, and symbiotic and pathogenic microbes.21,22 Third, owing to the endemic nature of human immunodeficiency virus, malaria, and tuberculosis in India, there is a continuous pathogenic assault to the immune system, leading to a proactive cell-mediated immune response. Fourth spices and herbs such as turmeric, cloves, ginger, mustard, saffron, cardamom, pepper, and garlic are essential ingredients in Indian cuisine. These spices are rich in bioactive compounds and phytochemical which possess medicinal antiviral and immunomodulatory properties.24 Fifth, chloroquine is used as an antimalarial in India and may possess immunomodulatory properties. Sixth, the Indian population manifests high genetic diversity in the human leukocyte antigen (HLA) complex, an immune response gene; this diversity is much more extensive than that in the Caucasian population—this diversity is attributed to a lifelong exposure among Indians to a high microbial load.25 Two single nucleotide polymorphisms—S19P (common in Africans) and K26R (common in Europeans)—can potentially affect the interaction between angiotensin converting enzyme-2 (ACE2) and the SARS-CoV-2 spike glycoprotein. While the former decreases ACE2 affinity for the spike protein and lowers viral susceptibility, the latter increases receptor affinity and predisposes to more severe disease.25 Hence, genetic polymorphisms in ACE2 receptors might be an important factor in determining susceptibility to SARS-CoV-2. Seventh, a unique micro-RNA (miRNA), hsa-mi R-27b, specifically targets the Indian SARS-CoV-2 genome; hsa-mi R-27b has not been detected in non indian population . It has been hypothesised that hsa-mi R-27b plays a specific defensive role against SARS-CoV-2 in the Indian population harbouring this unique sequence.26 These findings indicate a possible link between host miRNAs and disease severity as well as treatment outcomes. Eighth, Indians have a higher percentage of nature killer (NK) cells compared to that in other ethnic groups.27 It has been postulated that the development, tolerance, and activation of NK cells are regulated by killer cell immunoglobulin-like receptors (KIR) present on their surface. These receptors interact with the HLA class I molecules expressed by target cells and regulate cytolytic activity. While most KIRs are inhibitory and tend to suppress NK cell function, activating receptors such as KIR2DS1-5 and KIR3DS1 are upregulated in viral infections and host cell aberrations. All activating KIRs (except KIR2DS4) are encoded by the B haplotype, which is more prevalent in non-Caucasian populations such as Asian Indians than in Caucasian populations.28 Accordingly, Indians might have acquired activating KIR genes through a process of natural selection that
enabled them to survive epidemics during their pre-historic migrations from Africa.\textsuperscript{29} Ninth, live attenuated vaccines such as those for Bacillus Calmette-Guérin and mumps/measles/rubella (MMR) are commonly administered during childhood and have confer non-specific protection against unrelated lethal infections by inducing “trained” non-specific innate immune cells for a more efficient host response against a wide range of pathogens.\textsuperscript{13} The above points comprise interesting areas for active research. In addition to development of an ideal vaccine against SARS-CoV-2, having a trade off with time bioengineered antibodies and the use of computational method and laser microscopes for drug repurposing are additional exciting areas of research for therapeutics for COVID-19.

In southern Rajasthan, the following may have helped to control infection severity: 1) constructive coordination between various nodal and inter-nodal agencies of both the central and state government; 2) an aggressive response from the civic administration; public health agencies; medical, paramedical, and sanitation workers; and police and social law enforcement agencies; and 3) implementation of hand hygiene and social distancing measures. Active contact tracing was continued even when cases started to rise and at later stages—contact tracing in the COVID-19 pandemic is important even in advanced stages of the pandemic, as COVID-19 occurs in clusters and spreads, as opposed to influenza, which manifests waves of progression—this highlights the importance of contact tracing, even at advanced stages of the pandemic.

There are several study limitations, including the retrospective design and a setting of limited resources wherein all tests could not be performed for all patients.

**Conclusion**

This single-centre case series from the COVID care centre in Chitorgarh examined 353 hospitalised patients with COVID-19; 14 of these patients had severe COVID-19 pneumonia that required ICU care. Of these 14 patients, eight died, for a severe case fatality rate of 0.02. The most common symptoms were fever and cough, and the most common complications were ARDS, AKI, and multiple organ dysfunction syndrome. The current data strongly suggest that active contact tracing, even in the advanced stages of the pandemic, can control the spread and help mitigate the risk. More studies are required for using SOFA score as a surrogate marker for ICU care.

**Declaration of Conflicting Interests:** The authors declare that there is no Conflict of Interest.

**Declaration of Sources of Funding:** The authors having no sources of funding to declare and study was self funded.

**Ethical Committee Clearance:** Shri Sanwaliayaji District Hospital Chittorgarh/Rajasthan no:1/001/8/2020

**References**

7. Qiu J. Covert coronavirus infections could be seeding new outbreaks. Nature DOI: 10.1038/d41586-020-00822-x