Characteristics, Treatment Outcomes and Role of Hydroxychloroquine among 522 COVID-19 hospitalized patients in Jaipur City: An Epidemio-Clinical Study

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Abstract

Purpose: The present study was undertaken to investigate epidemiological distribution, clinical manifestation, co morbid status, treatment strategy and case fatality index of emerging COVID-19 infection at SMS Medical College Hospital, Jaipur, Rajasthan. It also evaluated efficacy of hydroxychloroquine (HCQ) in treatment of patients and risk of serious adverse outcomes in patients with COVID-19 in relation to their co morbid status.

Materials and methods: In an attempt to provide extensive information pertaining to epidemiological and clinical characteristics of COVID-19, the present study was undertaken on 522 patients. The patients were COVID-19 confirmed positive by genomic analysis through Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) at SMS Medical College and Attached Hospitals, Jaipur. The indoor admitted patient's information inclusive of demographic profile (age, sex, nationality, residence), date of confirmation for positive COVID-19 case, travel/ exposure history, date of recovery/ death, clinical features, co morbidities and treatment plan was recorded. A serial follow-up of recovered patients to evaluate infective period of the disease was also part of the study.

Results: A total of 522 patients of laboratory confirmed COVID-19 test by RT-PCR at SMS Hospitals, Jaipur were assessed. Among the confirmed cases, most of patients were young adult in the age group with mean age of 35.42 years. 22.41% patients were below 20 years of age, majority of patients (58.80%) were in the age range of 21 to 50 years and only 18.79% patient population was in the age range of above 50 years. Females (39.08%) were affected less than males (60.91%) with an average sex ratio of female: male being 0.64. Out of the total analyzed patients, only 24.32% patients were symptomatic, among them fever (55.90%), cough (52.75%), sore throat (49.60%) and shortness of breath (46.45%) were the most common presenting clinical manifestations while a few patients also had symptoms of headache (26.77%), chest pain (6.29%) and other symptoms (7.87%) like pain abdomen, fatigue, joints pain, altered sensorium etc. Most of symptomatic patients belonging to older age group. An average of 40.40% patient population of above 50 years of age, were symptomatic while none of the patients below 10 years of age were symptomatic. 13.98% patients had some or the other underlying co morbid disease. The most prevalent co morbidity was hypertension (42.46%) followed by Diabetes mellitus (39.72%), Old k-chest (20.54%), COPD/ Bronchial Asthma (16.43%), Coronary artery disease (13.69%), Chronic kidney disease (13.69%) and Valvular heart disease (6.84%) distributed in co morbid patients of COVID-19. 60.27% of patient population with underlying co morbid conditions were more prone to develop symptomatology complex as compared to that observed in patients with no co morbidity (18.42%). 116 patients had recovered with effective treatment till the date of data analysis. Time of recovery was counted from the date of positive report to 1st negative report of oropharyngeal sample by RT-PCR for COVID-19 with an average recovery time of 8.15 days. 23.27% patients recovered within 5 days, while 52.58% patients took about 6-10 days, 23.27% patients took 11-15 days and remaining 0.86% took more than 16 days to recover. In the present study 15 patients had died till analysis of data, among the deceased, 73.33% were above 50 year of age with a male preponderance (66.6%). Interestingly, all deceased (100%) had presented with clinical manifestations of COVID-19 and all had underlying multiple co morbid conditions. Majority of patients had early mortality after admission to hospital with two third death account in initial three days. Asymptomatic patients (cases) treated with HCQ recovered early (average recovery time =5.4 days) compared to asymptomatic patients who did not receive any treatment (control group) and had longer recovery time (average recovery time =7.6 days).

Conclusion: The varied spectra of COVID-19 mostly affects young adult age group (third to fifth decades of life). Interestingly, early age group was also affected in significant proportion when compared with similar data from other countries. It was observed that male population seemed to be was more prone to getting infected. Majority of COVID-19 positive patients (nearly three-fourth) were asymptomatic (mostly in young age range) at the time of diagnosis, which poses a major challenge for health care workers. Fever, cough, sore throat and shortness of breath were major symptoms that could be detected in such COVID-19 patients. Symptomatic clinical manifestations were more common in old age population. Infectivity was higher in patients that had underlying co morbid disease, especially in patients with multiple co morbid conditions. Symptomatic presentation of COVID-19 was observed to be higher in patients with co morbid disease. Average recovery time from COVID-19 was 8 days with effective treatment. Mortality in COVID-19 was higher in old age population, male gender, symptomatic and co morbid patients as compared to other similarly matched group. Most of mortality was noted within first few days of admission, suggestive of early mortality due to the primary disease process. Treatment with HCQ had early recovery without effectively influencing the overall mortality.

Introduction

Since November 2019, the rapid outbreak of coronavirus disease 2019 (COVID-19), which arose from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, has become a public health emergency of international concern (1). COVID-19 has contributed to an enormous adverse impact globally. Infection by COVID-19 can result in a range of clinical outcomes, from asymptomatic to severe life-threatening course or death. Characterization of epidemiological, clinical, co morbid features with recovery and mortality of COVID-19 is crucial for development and implementation of effective control strategies and management protocol. If well tracked and monitored early in its time-course, early characterization of an emerging pathogen provides a unique opportunity to understand its transmission, natural history, and effectiveness of screening, though plausibility of making such assumptions relating to time course and geographic locales become far-fetched when the pathogen has spread-over with full temerity. Based on current epidemiological investigation, the incubation period of COVDI-19 seems to be 1–14 days, mostly 3–7 days. COVID-19 is contagious during its latency period (2). It is highly transmissible in humans, especially in the elderly and people with underlying diseases. As per literature median age of patients is 47–59 years with around 41.9–45.7% of patient population being of female gender (3). The clinical manifestations of COVID-19 are heterogeneous (4) with fever, cough, sore throat, shortness of breath, headache, fatigue, abdominal discomfort being the predominant features. On admission, many patients have reported as having at least one co morbidity with diabetes, hypertension, and cardiovascular and cerebrovascular diseases being most commonly reported conditions (4,5). Similar with influenza, Severe Acute Respiratory Syndrome coronavirus (SARS-CoV) (6) and Middle East Respiratory Syndrome coronavirus (MERS-CoV) (7), COVID-19 more readily predisposes to respiratory failure and death in susceptible patients (4). Recovery and mortality of patients from COVID-19 is influenced by their respiratory system involvement and other systemic manifestations. In the present study clinical data of 522 patients admitted to SMS Medical College Hospital, Jaipur, Rajasthan with laboratory-confirmed COVID-19 test were analyzed with the objective being to evaluate epidemiological characteristics, clinical features, co morbidity status and outcome of COVID-19 with its prognostic and diagnostic correlation and implications.

Method

Study Design: The present descriptive, retrospective analysis was done on COVID-19 positive patients admitted to S.M.S. Medical College Hospital, Jaipur, Rajasthan from last week of February, 2020 to April 20, 2020, when COVID-19 was declared a public health emergency of pandemic proportions and subsequently formal screening and diagnostic investigations for SARS-CoV-2 was initiated throughout India. The privacy and confidentiality of patients was observed as per norms.

Data Collection

After collection of all required data and careful medical chart review, the clinical data of laboratory-confirmed 522 hospitalized patients till 20th April 2020 was compiled and tabulated. The diagnosis of COVID-19 was made based on the World Health Organization interim guidance, wherein confirmed cases denoted were patients whose RT-PCR assay findings for nasal and pharyngeal swab specimens were positive (3). The epidemiological data (age, sex, residence) was recorded and clinical data, inclusive of recent exposure history, clinical symptoms and signs, co morbidities, was obtained. The admitted patients were serially followed up for their symptomatology complex, with recovery of patients being confirmed with first negative oropharyngeal or nasopharyngeal sample by RT-PCR for COVID-19. This concept was based on seroconversion in COVID-19 patients. The primary endpoint of the study was a composite measure which consisted with negativity of first COVID-19 sample or death of patient.

COVID-19 positive patients were treated with Lopinavir/Ritonavir, Hydroxychloroquine (HCQ), Azithromycin and symptomatically accordingly.

Variables: The patient characteristics were collected at baseline and confirmed cases were diagnosed based on positive viral nucleic acid test result on throat swab samples. The variables evaluated included age and gender distribution, clinical manifestations, co morbid status, recovery trending in terms of time and resolution of symptoms, death of patients and their correlation with each other and were categorized for analysis and necessary preventive and curative protocol was initiated. Age distribution graphs were constructed and sex ratio (i.e., male: female [M:F] ratio) was calculated. The clinical profile of COVID-19 positive patients was evaluated in terms of percentage prevalence in relation to age group of patients. Co morbid status of patients was documented as percentage prevalence of COVID-19 in such patients and its correlation with symptomatic presentation and mortality of patients. Recovery of patients was analyzed as time duration of date of positive sample to first negative sample by RT-PCR for COVID-19. Mortality of patients was analyzed with respect to time duration from admission, age group and gender of deceased and association, if any, with symptomatic presentation and ante mortem co morbidity. Treatment of patients was based on a rationale protocol of decreasing viral load. In the follow-up study of a total of 131 patients, severity of COVID-19 was segregated into critically ill, severely ill, mildly ill and asymptomatic category (8). The patients were treated according to their severity and divided into (1) Group A for critically ill patients treated with *Lopinavir and Ritonavir*, (2) Group B for severely ill patients treated with *HCQ and Azithromycin*, (3) Group C for mildly ill patients treated with HCQ alone, (4) Group D for asymptomatic patients treated with HCQ alone and (5) Group E for asymptomatic patients without any proposed definitive treatment (HCQ not received by this group due to some contraindication or refusal by patients/attender). To study effect of HCQ on prognosis of patients, asymptomatic COVID-19 positive patients were further sub divided into two categories, with and without HCQ, into Group D and Group E considered as Case and Control respectively for this study.

The Rationale of Putative Definitive Management Protocol of COVID-19

SARS-CoV-2 is a virus belonging to coronavirus family and has a propensity to access pulmonary portal via *angiotensin converting enzyme receptor 2 (ACE2)* or *basigin* mediated entry (9) and has four structural proteins namely S (spike), E (envelope), M (membrane) and N (nucleocapsid) (10). The entry of virus is also facilitated by proteases of host cells. Considering the entry of virus and its initiation into host cell through proteases, the concept of designing a definitive management protocol primarily targeting the entry point and protease facilitator was evolved. Subsequently, use of antiretroviral drugs *Lopinavir and Ritonavir*, approved for use in patients afflicted with *Human Immunodeficiency Virus (HIV)* (11), as protease inhibitors (moreover documentation of genome similarity of SARS-CoV-2 HIV (12) and that of *HCQ* as its inhibitory action on respiratory angiotensin converting enzyme receptor (ACE2), the portal and receptor of entry of SARS-CoV-2 (13). The macrolide *azithromycin* was included as part of management protocol due to its inhibitory action on protein biosynthesis, anti-inflammatory, anti-cytokine actions and presentation with different invasion inhibitory activity (14).

Statistical analysis

The present hospital based, observational descriptive study conducted on 522 COVID-19 patients at SMS Medical College Hospital, Jaipur to investigate epidemiological distribution, clinical manifestation, co morbid status, treatment strategy and case fatality index of emerging COVID-19 infection at SMS Medical College Hospital, Jaipur, Rajasthan. The efficacy of hydroxychloroquine (HCQ) in treatment of patients and risk of serious adverse outcomes in patients with COVID-19 in relation to their co morbid status was also undertaken. The descriptive statistics for quantitative data was expressed as mean and standard deviation and qualitative data was expressed as proportions.

Results

Serial data from COVID-19 positive patients were collected, evaluated, interpreted and correlated with each other and with clinico-epidemiological variables of age, sex, clinical features, co morbidity, recovery and mortality.

A total of 522 laboratory confirmed COVID-19 patients by RT-PCR admitted at SMS Medical College Hospital, Jaipur, Rajasthan till 20th April 2020, were assessed. Among the confirmed cases, most of patients were young adult in the age group with mean age of 35.42 years. 22.41% patients were below 20 years of age, majority of patients (58.80%) were in the age range of 20 to 50 years and only 18.79% patient population was in the age range of above 50 years. Proportional distribution of patients according to age group was found as 0-10 year 0.065 (95% CI = 0.046-0.09), 10-20 year 0.159 (95% CI = 0.129-0.193), 20-30 year 0.257 (95% CI = 0.22-0.296), 30-40 year 0.192 (95% CI = 0.159-0.228), 40-50 year 0.14 (95% CI = 0.111-0.173), 50-60 year 0.098 (95% CI = 0.074-0.126), 60-70 year 0.063 (95% CI = 0.044-0.088), 70-80 year 0.015 (95% CI = 0.007-0.03), Above 80 year 0.011 (95% CI = 0.004-0.025) (*graph 1*). Females {39.08% (95 % CI = 34.9% - 43.4%)} were affected less than males {60.91% (95 % CI = 56.36% - 65.1%)} with an average sex ratio of female: male being 0.64 (*graph 2*).

In the present study a total of 522 patients were analyzed and among them only 127 patients {24.32% (95% CI = 19.6 – 26.9)} were symptomatic while remaining 395 patients {75.68% (95% CI = 73.0 – 80.2)} had no clinical manifestations at presentation (*graph 3*). In symptomatic patients, fever (55.90%), cough (52.75%), sore throat (49.60%) and shortness of breath (46.45%) were most common presenting clinical manifestations while few patients also presented with headache (26.77%), chest pain (6.29%) and other non-specific symptoms (7.87%) like pain abdomen, fatigue, joints pain, altered sensorium, etc. (*graph 4*). Symptomatic presentation in COVID-19 was also dependent on age profile of patients with most of symptomatic patients (40.40%) being in old age group of above 50 years, while none of patients of below 10 years of age were symptomatic (*graph 5*). In the study population 73 patients {13.98% (95% CI = 11.1 – 17.2%)} had underlying co morbid disease. Multiple co morbid disease was more prevalent (57.53%) among co morbid population. The most prevalent co morbidity observed in the sample population co morbid patients of COVID-19 was hypertension (42.46%) followed by Diabetes mellitus (39.72%), Old k-chest (20.54%), COPD/Bronchial Asthma (16.43%), Coronary artery disease (13.69%), Chronic kidney disease (13.69%) and Valvular heat disease (6.84%), while co morbid disease percent distribution in whole sample population was noted as 5.93% for HTN, 5.55% for T2DM, 2.87% for Old k-chest, 2.29% for COPD/ Bronchial Asthma, 1.91% for CKD, 1.91% for CAD-LVF and 0.95% for RHD-MS-MR (*graph 6*). COVID-19 patients who had underlying co morbid conditions were more prone to develop symptomatic disease (60.27%) as compared to that observed in such patients with no co morbid conditions (18.42%) (*graph 7*). In the present study 116 patients recovered with effective treatment at the time of data analysis. Time duration needed for recovery was assessed as time elapsed between date of positive report to 1st negative report of oropharyngeal/ nasopharyngeal sample by RT-PCR for COVID-19. An average recovery time of 8.15 days was observed. 23.27% patients recovered within 5 days, while 52.58% patients took 6-10 days, 23.27% patients took 11-15 days and remaining 0.86% took more than 16 days to recover (*graph 8*). In the present study 15 patients succumbed to life and died due to COVID related illness, among the deceased 73.33% were above 50 years of age with a male preponderance (66.6%). Interestingly all deceased (100%) presented with clinical manifestation of COVID-19 and all had underlying multiple co morbid conditions (*table 1*). Majority of patients had early mortality after admission in the Hospital and accounted for 13.33% of death on first day of admission, 40% of mortality was observed on second day, 13.33% on third day, 13.33% on fourth day, 6.66% on fifth day and 13.33% mortality was observed after sixth day of admission (*graph 9*). In the follow-up study of a total 131 patients were categorized by severity of disease into critically ill, severely ill, mildly ill and asymptomatic patients of COVID-19. Patients treated according to their severity were categorized as (1) Group A inclusive of critically ill patients treated with Lopinavir and Ritonavir, (2) Group B included severely ill patients treated with HCQ and Azithromycin, (3) Group C had mildly ill patients treated with HCQ alone, (4) Group D was inclusive of asymptomatic patients treated with HCQ alone and (5) Group E included asymptomatic patients receiving only symptomatic and no proposed definitive treatment (HCQ not received by this group due to some contraindication or refusal by patients/attender). To see effect of HCQ on prognosis of patients, asymptomatic COVID-19 positive patients were divided into two categories on the basis of treatment that was categorized as Group D and Group E considered as Case and Control respectively for this study. In the present study, Group A had 9 patients, Group B had 16 patients, Group C had 25 patients, Group D had 44 patients and Group E had 37 patients and among them percentage recovered patients were 44.44%, 64.70%, 93.93%, 97.50% and 96.85% for each group, respectively (*graph 10*) with an average recovery time of 16.1 Day, 14.3 Day, 10.1 Day, 5.4 Day, 7.6 Day, respectively for each group. Asymptomatic patients (case) treated with HCQ recovered early (average recovery time = 5.4 days) as compared to that observed in asymptomatic patients who did not receive any specific proposed treatment (control group) and had longer recovery time (average recovery time =7.6 days). The difference of percentage of recovered patients in the two groups categorized as case and control was not statistically significant (*table 2*).

Discussion

The dread and specter of COVID-19 made its first appearance in Wuhan, China and it has spread like wildfire out and across precincts of China and across the globe with a pace that has taken everyone by surprise. Confirmed cases of COVID-19 is being reported from all corners of the world and subsequently World Health Organization (WHO) officially declared COVID-19 a pandemic on March 11, 2020 (15). Research is underway to understand more about transmissibility, severity, and other features associated with COVID-19 (16). The virus, SARS-CoV-2, of COVID-19 has been found to have higher levels of transmissibility with higher potential of pandemicity, as the effective reproductive number (R) of COVID-19 (2.9) is estimated to be higher than the reported effective reproduction number (R) of SARS (1.77) at this early stage (17). The SARS-related coronaviruses are covered by spike proteins that contain a variable receptor-binding domain (RBD). This RBD binds to angiotensin-converting enzyme-2 (ACE-2) receptor found in the heart, lungs, kidneys, and gastrointestinal tract (18) thus facilitating viral entry into target cells. Based on genomic sequencing, the RBD of SARS-CoV-2 appears to be a mutated version of its most closely related virus, RaTG13, sampled from bats (Rhinolophus affinis) (19). The mutation increased the RBD affinity to ACE-2 in humans. Binding of the SARS-CoV to the angiotensin-converting enzyme 2 (ACE-2) receptors in the type II pneumocytes in the lungs triggers a cascade of inflammation in the lower respiratory tract (20). It has been demonstrated that when the SARS spike protein binds to the ACE-2 receptor Pathogens, the complex is proteolytically processed by type 2 transmembrane protease TMPRSS2 leading to cleavage of ACE-2 and activation of the spike protein (21), similar to the mechanism employed by influenza and human metapneumovirus, thus facilitating viral entry into the target cell. It has been suggested that cells in which ACE-2 and TMPRSS2 are simultaneously present are most susceptible to entry by SARS-CoV (22). Early indications are that SARS-CoV-2 virus also requires ACE-2 and TMPRSS2 to enter cells (23). Viral entry and cell infection trigger the host's immune response, and the inflammatory cascade is initiated by antigen-presenting cells (APC). The process starts with the APC performing two functions: (1) presenting the foreign antigen to CD4 +-T-helper (Th1) cells, and (2) releasing interleukin-12 to further stimulate the Th1 cell. The Th1 cells stimulate CD8 +-T-killer (Tk) cells that will target any cells containing the foreign antigen. In addition, activated Th1 cells stimulate B-cells to produce antigen-specific antibodies. It is apparent that COVID-19 infection occurs through exposure to the virus, and both immune suppressed and normal population appear to be susceptible. Some studies have reported an age distribution of adult patients between 25 and 89 years old. Most adult patients to be afflicted have been observed to be in age range of 35 and 55 years (24). A study on early transmission dynamics of the virus has reported the median age of patients to be 59 years, ranging from 15 to 89 years, with majority (59%) patients affected being male (25). It has been suggested that population most at risk may be people with poor immune function such as older people and those with renal and hepatic dysfunction (25).

In the present study an attempt was made to outline distribution of age, gender, clinical features at presentation, co morbidity of patients, response of COVID-19 patients to putative definitive management protocol so designed

and formulated with the premise of inhibiting intracellular receptor-mediated entry of SARS-CoV-2 and targeted protein synthesis within the cells and cells of inflammation within respiratory system. A total of 522 patients were analyzed and 131 patients were followed-up along the course of the study and among them 116 patients recovered and 15 patients succumbed to life. Most of COVID-19 patients admitted to SMS Medical College Hospital, Jaipur, Rajasthan were young adults with a mean age of 35.42 year and male gender was affected more as compared to females, with an average sex ratio being 0.64. The mean age (35.42 year) of affected patients was significantly low in the sample COVID-19 patient population as compared to that documented from other countries (12). Around three fourth of COVID-19 positive patients were asymptomatic at time of hospital admission. The small percentage of asymptomatic COVID-19 patients, acting as major carrier for transmission of virus in society, poses a real diagnostic and containment challenge for health care professionals.

In symptomatic patients, fever and cough were the most common presenting features, followed by sore throat, shortness of breath and headache while few patients also presented with chest pain and non-respiratory symptoms like pain abdomen, fatigue, joints pain, altered sensorium, etc. Symptomatic presentation in COVID-19 was also dependent on age profile of patients with most of symptomatic patients (about 40.40%) falling in the age range above 50 years of age, while none of patients below 10 years of age were symptomatic. The pediatric age group poses a real challenge for community in terms of adherence to preventive measures.

It was observed in the present study co morbidities have a tangible impact on clinical characteristics and course in COVID-19 positive patients. It has been observed that COVID-19 patients have circulatory and endocrine co morbidities. Patients with at least one or more co morbidity have been reported with poor clinical outcomes. Notwithstanding the commonness of circulatory and endocrine co morbidities, patients with COVID-19 rarely have co morbid respiratory diseases (particularly COPD). In the present study population 13.98% patients had underlying co morbid disease with multiple co morbid diseases being was more prevalent. The most prevalent co morbidity observed in present study was hypertension followed by Diabetes mellitus, Old k-chest, COPD/Bronchial Asthma, Coronary artery disease, Chronic kidney disease and Valvular heat disease. Nearly about 60% COVID-19 patients who had underlying co morbid conditions developed symptomatic disease while only 18% non-co morbid patients developed symptomatic disease.

In follow-up series of COVID-19 patients, it was observed that most of patients recovered while few patients succumbed to the disease process with an average recovery to mortality ratio in given time period being 7.33. The recovery time of COVID patients was variable and it was observed to be dependent on patients' age, sex, clinical presentation and underlying co morbid condition. The first seroconversion of first negative report of COVID-19 by RT-PCR defined overall healthcare burden with average hospital stay duration and concomitant appointment of healthcare personnel. In COVID-19 related deaths, major concern was ageing population of above 50 years with a predilection for male gender, necessitating the need to prioritize such a population cohort in order to minimize fatality rates of COVID-19. Interestingly all deceased present had clinical manifestations of COVID-19 and underlying multiple co morbid conditions. It was observed that fatalities in COVID-19, when they occur, are rapid and swift and take place early within few days of hospital admission. It was also observed that patient recovery rates were lowest in critically ill patients and highest in asymptomatic patients. As for efficacy of HCQ in asymptomatic COVID-19, the proportion of recovered asymptomatic patients who were on HCQ was slightly higher than those of control group (asymptomatic COVID-19 positive patients without any treatment). Recovery duration was maximum for critically ill patients followed by severely ill, mild symptomatic, asymptomatic without treatment and asymptomatic on HCQ in decreasing order.

Conclusion

It could be concluded that spectrum of COVID-19 mostly affects young adult age group (third to fifth decades of life), a finding that contrasts with documentations from other countries. The percentage of male gender to be afflicted with COVID-19 was more. Majority of patients (nearly three-fourth) of COVID-19 disease were asymptomatic at the time of diagnosis and presentation. Symptomatic presentation was more common in old age population. Infectivity was higher in patients who had underlying co morbid diseases especially with multiple co morbid diseases. The average recovery time from COVID-19 was 8 days with effective treatment. Mortality in COVID-19 was higher in old age population, male gender, symptomatic and in patients with co-existing co morbid conditions. Most of mortality was noted within in few days of admission suggestive of early mortality due to primary disease. The recovery percentage was lowest with recovery duration being maximum in critically ill patients and the opposite trending was observed in asymptomatic patients on HCQ treatment. It was observed that putative definitive management protocol with HCQ enhances the chances of early recovery, modulating the overall mortality profile of COVID-19.

Limitations

The limitations of the study include its small sample population size with lack of complete follow-up. **Ethical approval:** Approval was not required.

Author contributions: S. Bhandari, A. Singh and G. Rankawat formulated the research questions, designed the study, developed the preliminary search strategy, and drafted the manuscript; S. Bhandari, G. Rankawat, R. Sharma refined the search strategy by conducting interative database queries and incorporating new search terms; G. Rankawat, A. Dube, S. Kakkar. A. Talk, V. Gupta, S. Sharma collected and analysed data; S. Bhandari and A. Singh, A. Agrawal conducted the quality assessment. All authors critically reviewed the manuscript for relevant intellectual content. All authors have read and approved the final version of the manuscript.

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Declaration of competing interest: All authors report no potential conflicts. All authors have submitted the ICMJE Form for Disclosure of Potential.

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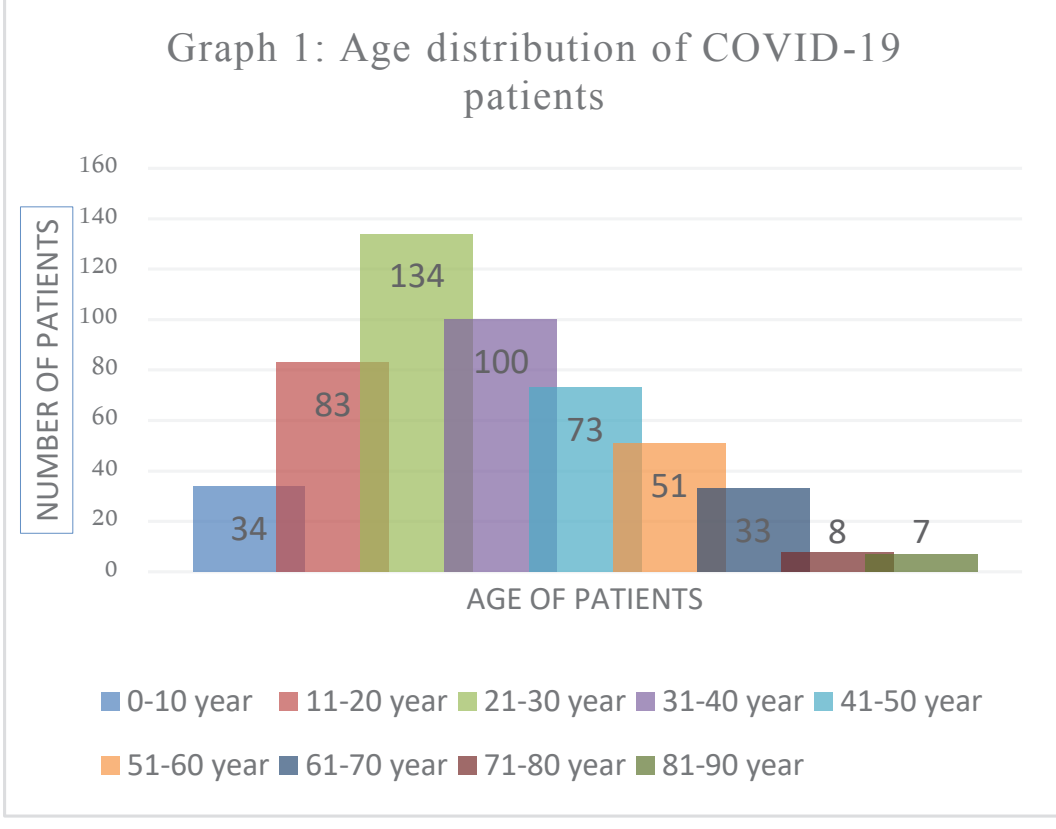
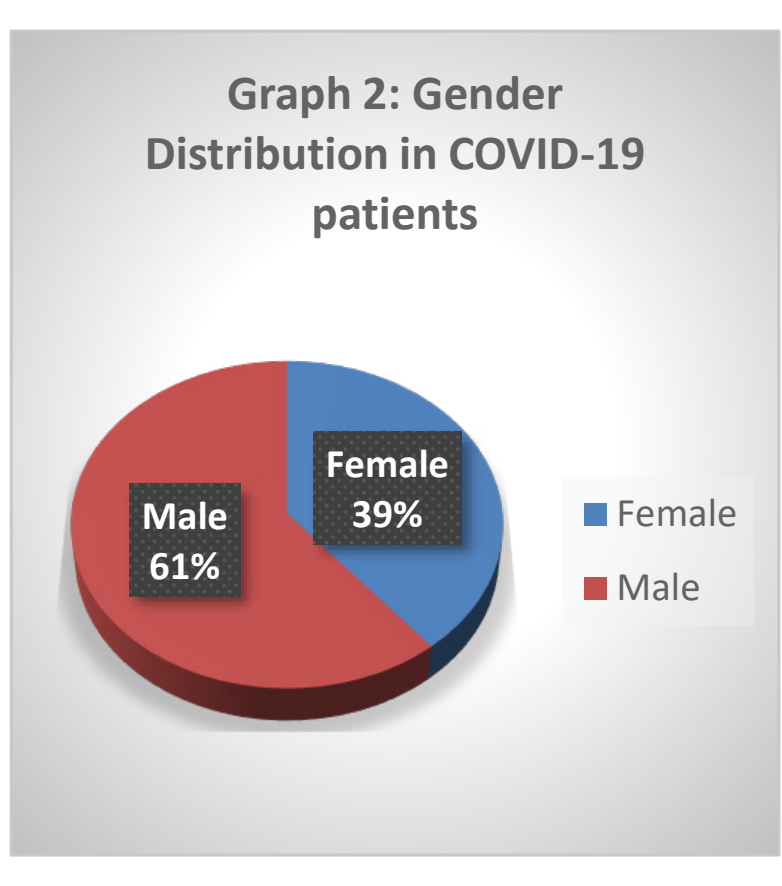
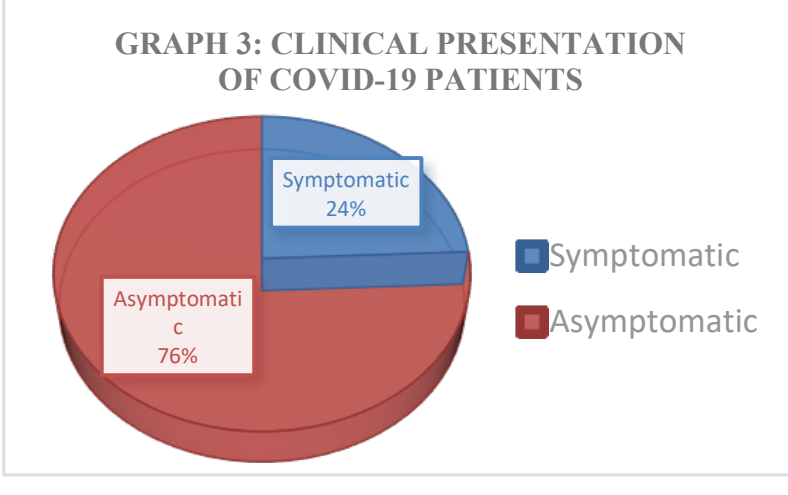


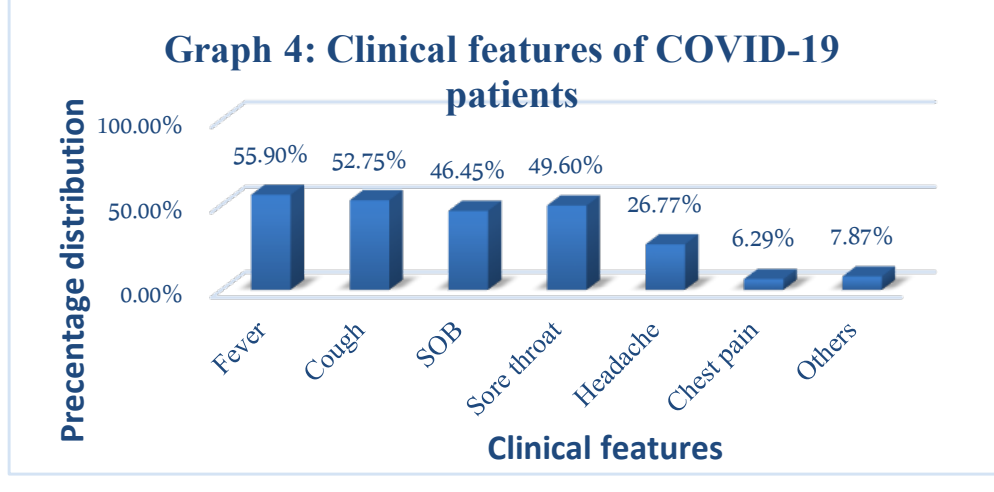
Graph 1: Age distribution of COVID-19 patients



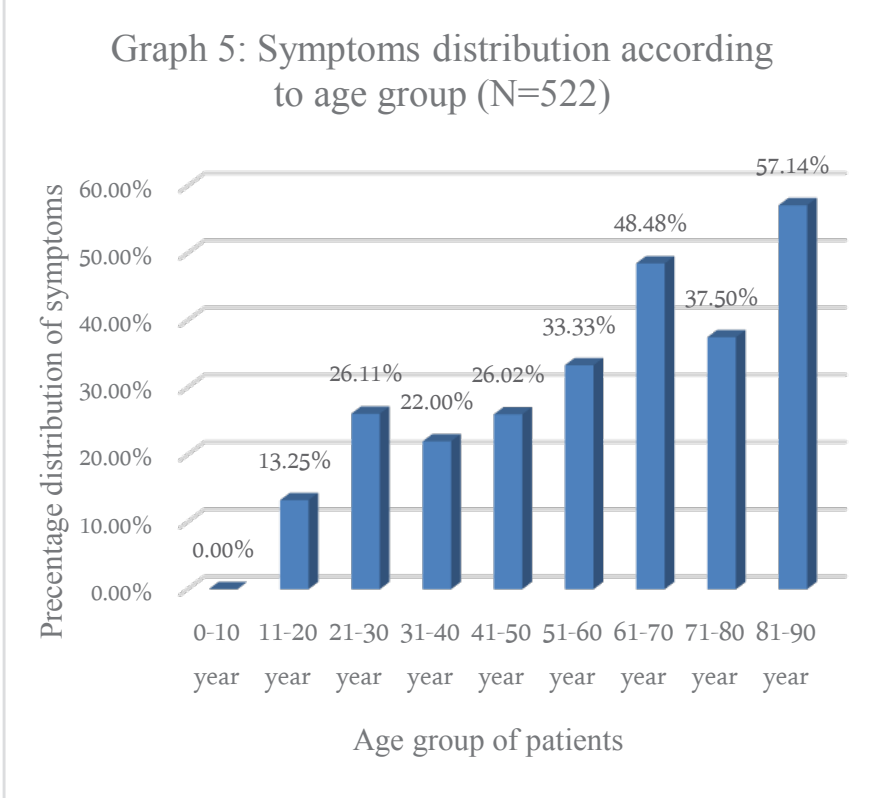
Graph 2: Gender Distribution in COVID-19 patients



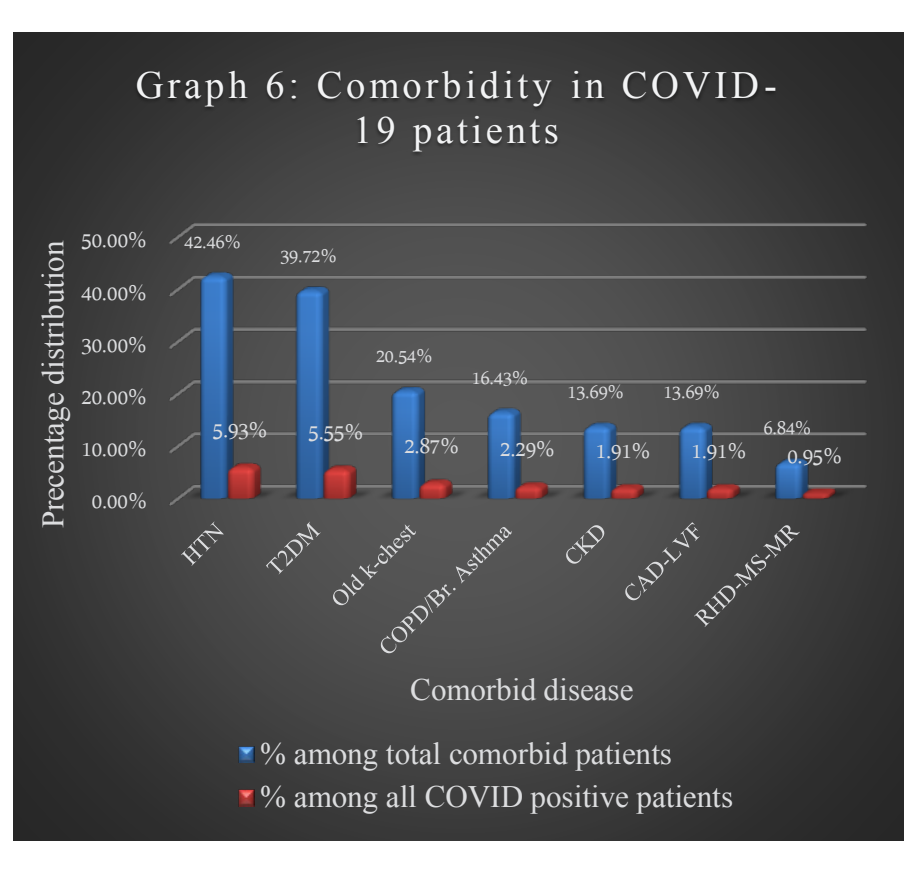
GRAPH 3: CLINICAL PRESENTATION OF COVID-19 PATIENTS



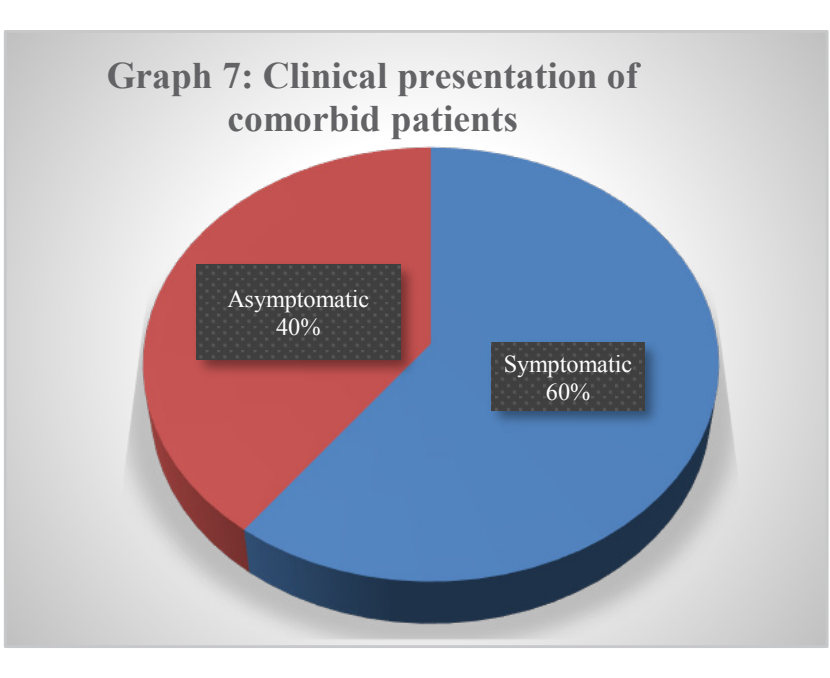
Graph 4: Clinical features of COVID-19 patients



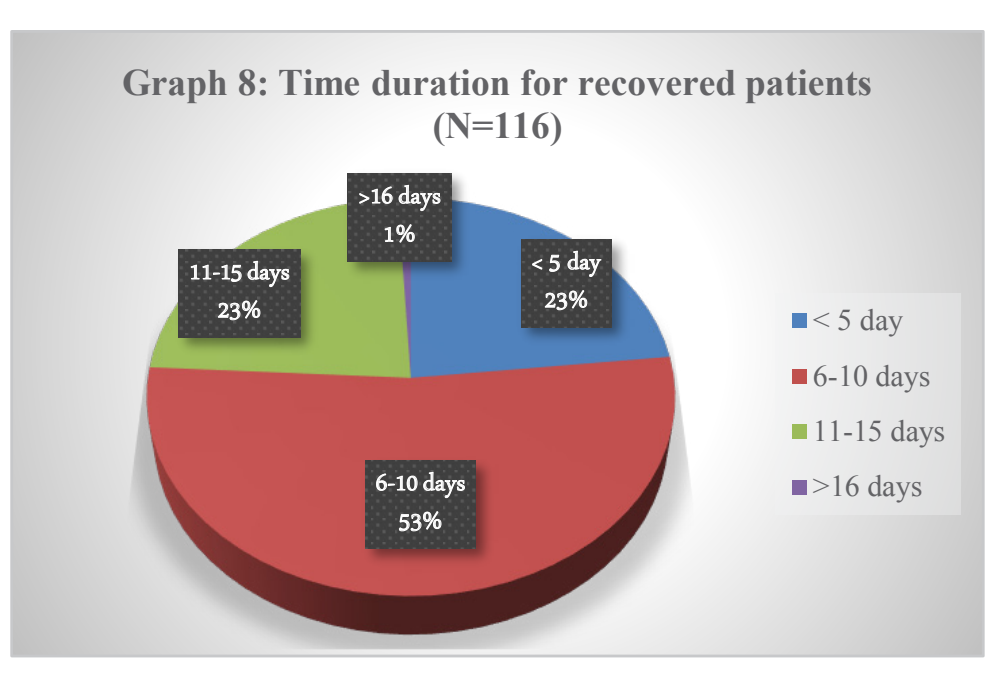
Graph 5: Symptoms distribution according to age group (N=522)



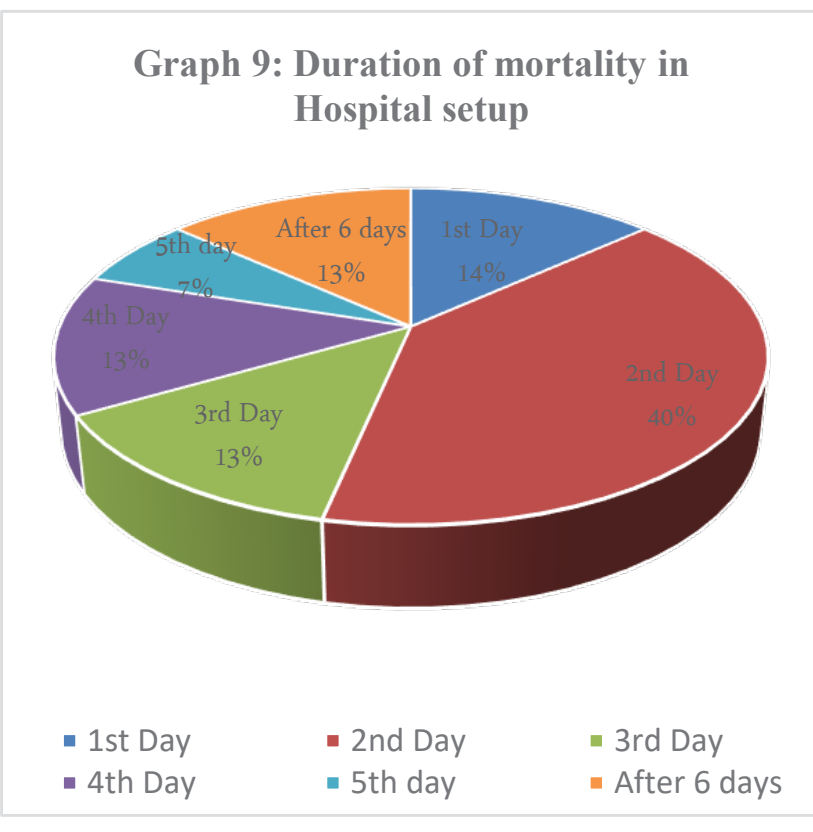
Graph 6: Comorbidity in COVID-19 patients



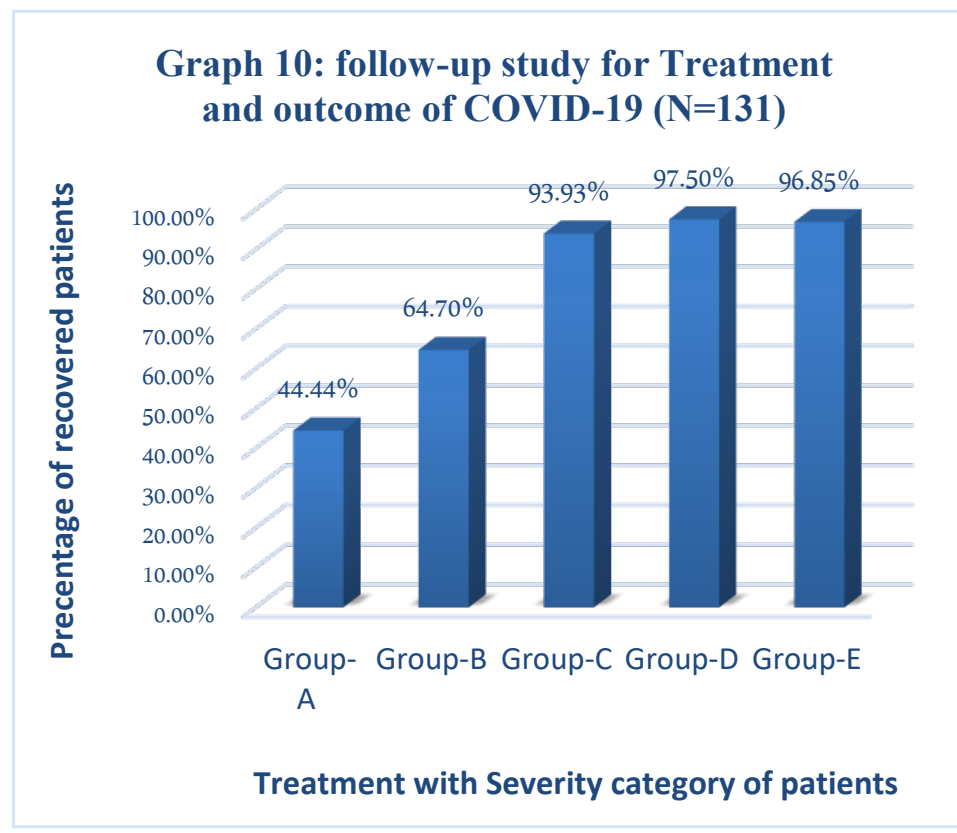
Graph 7: Clinical presentation of comorbid patients



Graph 8: Time duration for recovered patients (N=116)



Graph 9: Duration of mortality in Hospital setup



Graph 10: follow-up study for Treatment and outcome of COVID-19 (N=131)

Table 1: Epidemiology, time duration, Clinical features and comorbidity of deceased (in 15 COVID-19 related deaths in Hospital setup)

							Clinical manifestation						
S. no.	Age (year)	Se x	Contact history	Date of admission	Date of death	Outcome	Cough	Fever	S O B	Sore throat	Head ache	Others	Comorbid status
1	85	M	Yes	01.04.2020	02.04.2020	DEATH	√	√	√	√	√	Chest pain	HTN, T2DM
2	82	M	Yes	04.04.2020	05.04.2020	DEATH	-	√	√	√	√	-	COPD, CAD-LVF
3	65	F	Yes	08.04.2020	09.04.2020	DEATH	-	√	√	√	-	Chest pain	COPD, HTN
4	65	M	Yes	11.04.2020	15.04.2020	DEATH	√	√	√	√	√	Chest pain	T2DM, Myocarditis, HFrEF=35%
5	64	F	Yes	09.04.2020	15.04.2020	DEATH	√	√	√	√	√	-	T2DM, HTN, Br. Asthma
6	62	M	Yes	10.04.2020	10.04.2020	DEATH	√	√	√	√	√	Chest pain	HTN, T2DM, COPD
7	70	M	Yes	11.04.2020	19.04.2020	DEATH	√	√	√	√	-	-	HTN, T2DM
8	13	F	No	09.04.2020	11.02.2020	DEATH	√	√	√	√	√	-	Bronchial asthma
9	76	M	Yes	13.04.2020	17.04.2020	DEATH	√	√	√	√	√	-	HTN, BPH
10	22	M	Yes	14.04.2020	17.04.2020	DEATH	√	√	√	√	√	-	RHD-MS-MR
11	60	F	Yes	13.04.2020	14.04.2020	DEATH	√	√	√	-	-	-	T2DM, CKD,
12	53	M	Yes	17.04.2020	18.04.2020	DEATH	√	-	√	√	√	-	T2DM, HTN,
13	47	M	Yes	13.04.2020	18.04.2020	DEATH	√	√	√	√	√		T2DM
14	48	F	Yes	17.04.2020	17.04.2020	DEATH	√	√	√	√	-	Chest pain	CAD-ACS-LVF
15	62	M	Yes	18.04.2020	19.04.2020	DEATH	-	√	√	√	√	Altered sensorium	T2DM, CKD

Table 2: Treatment and outcome strategy in 131 follow-up patients of sample population showing categorization of patients according to severity and treatment, average recovery time with percentage recovered patients

Follow-up study for Treatment and outcome of COVID-19 (N=131)								
S. No.	Group	Patients category	Medicine	No. of patients	Recovered Patients	Death	Average Recovery time	% of Recovered Patients
1	A	Critically ill	Lopinavir + Ritonavir	9	4	5	16.1 Day	44.44%
2	B	Severely ill	HCQ + Azithromycin	17	11	6	12.6 Day	64.70%
3	C	Mild ill	HCQ	33	31	2	10 Day	93.93%
4	D	Asymptomatic	HCQ	40	39	1	5 Day	97.50%
5	E	Asymptomatic	None	32	31	1	7.5 Day	96.85%

References

1. WHO main website. https://www.who.int (accessed March 10th, 2020)
2. Jin YH, Cai L, Cheng ZS, Cheng H, Deng T, Fan YP, et al. A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019nCoV) infected pneumonia (standard version). Mil Med Res. 2020;7(1):4.
3. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. N Engl J Med. 2020. https://doi.org/10.1056/NEJMoa2001316 [Epub ahead of print].
4. Huang C, Wang Y, Li X, et al. Clinical features of patients with 2019 novel coronavirus in Wuhan, China. Lancet. 2020; doi: 10.1016/S0140-6736(20)30183-5
5. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet. 2020. doi: 10.1016/S0140-6736(20)30211-7
6. Booth CM, Matukas LM, Tomlinson GA, et al. Clinical features and short-term outcomes of 144 patients with SARS in the greater Toronto area. JAMA. 2003;289:2801-2809
7. Alqahtani FY, Aleanizy FS, Ali Hadi Mohammed R, et al. Prevalence of comorbidities in cases of Middle East respiratory syndrome coronavirus: a retrospective study. Epidemiol Infect. 2018;5:1-5
8. Wu Z, McGoogan JM. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention. JAMA 2020.
9. Wang K, Chen W, Zhou YS, et al. SARS-CoV-2 invades host cells via a novel route: CD147-spike protein. BioRxiv preprint. 2020 doi: 10.1101/2020.03.14.988345. [CrossRef] [Google Scholar]
10. Yan R, Zhang Y, Li Y, et al. Structural basis for the recognition of the SARS-CoV-2 by full-length human ACE2. Science. 2020 doi: 10.1126/science.abb2762. [PMC free article] [PubMed] [CrossRef] [Google Scholar].
11. HIV/AIDS Treatment Information Service Guidelines for the efavirenz: one-year safety/efficacy evaluation and phenotypic use of antiretroviral agents in HIV-infected adults and adoles- breakpoints in multiple-PI-experienced patients [abstract no. cents [online]. Available from URL: http://www.hivatis.org 525]. 8th Conference on Retroviruses and Opportunistic Infec- [Accessed 2003 Mar 7].
12. Sin-Yee Fung, Kit-San Yuen, Zi-Wei Ye, Chi-Ping Chan & Dong-Yan Jin (2020) A tug-of-war between severe acute respiratory syndrome coronavirus 2 and host antiviral defence: lessons from other pathogenic viruses, Emerging Microbes & Infections, 9:1, 558-570, DOI: 10.1080/22221751.2020.1736644: https://doi.org/10.1080/22221751.2020.1736644.
13. Al-Bari MA. Chloroquine analogues in drug discovery: new directions of uses, mechanisms of actions and toxic manifestations from malaria to multifarious diseases. J Antimicrob Chemother. 2015;70(6):1608– 1621. DOI:10.1093/jac/dkv018.
14. Wilson DW, Goodman CD, Sleebs BE, et al. Macrolides rapidly inhibit red blood cell invasion by the human malaria parasite, Plasmodium falciparum. BMC Biology. 2015;13:52. doi: 10.1186/s12915-015-0162-0. [PMC free article] [PubMed] [CrossRef] [Google Scholar].
15. Coronavirus (COVID-19) events as they happen (n.d.). https://www.who.int/emergencies/diseases/novel-coronavirus-2019/events-as-they-happen(Accessed 20March2020).
16. CDC. 2019 Novel coronavirus, Wuhan, China. 2020. https://www.cdc.gov/coronavirus/2019-nCoV/summary.html. Accessed 1 Feb 2020.
17. Liu T, Hu J, Kang M, Lin L, Zhong H, Xiao J, et al. Transmission dynamics of 2019 novel coronavirus (2019-nCoV). 2020; doi: https://doi.org/10.1101/2020.01.25.919787.
18. Ksiazek, T.G.; Erdman, D.; Goldsmith, C.S.; Zaki, S.R.; Peret, T.; Emery, S.; Tong, S.; Urbani, C.; Comer, J.A.; Lim, W.; et al. A Novel Coronavirus Associated with Severe Acute Respiratory Syndrome. N. Engl. J. Med. 2003, 348, 1953–1966. [CrossRef] [PubMed]
19. Andersen, K.; Rambaut, A.; Lipkin, W.I.; Holmes, E.C.; Garry, R.F. The Proximal Origin of SARS-CoV-2. Available online: http://virological.org/t/the-proximal-origin-of-sars-cov-2/398 (accessed on 25 February 2020).
20. Kuba, K.; Imai, Y.; Rao, S.; Gao, H.; Guo, F.; Guan, B.; Huan, Y.; Yang, P.; Zhang, Y.; Deng, W.; et al. A crucial role of angiotensin converting enzyme 2 (ACE2) in SARS coronavirus–induced lung injury. Nat. Med. 2005, 11, 875–879. [CrossRef] [PubMed]
21. Glowacka, I.; Bertram, S.; Muller, M.A.; Allen, P.; Soilleux, E.; Pfefferle, S.; Steffen, I.; Tsegaye, T.S.; He, Y.; Gnirss, K.; et al. Evidence that TMPRSS2 Activates the Severe Acute Respiratory Syndrome Coronavirus Spike Protein for Membrane Fusion and Reduces Viral Control by the Humoral Immune Response. J. Virol. 2011, 85, 4122–4134. [CrossRef]
22. Shulla, A.; Heald-Sargent, T.; Subramanya, G.; Zhao, J.; Perlman, S.; Gallagher, T. A Transmembrane Serine Protease Is Linked to the Severe Acute Respiratory Syndrome Coronavirus Receptor and Activates Virus Entry. J. Virol. 2011, 85, 873–882. [CrossRef]
23. Zhou, P.; Yang, X.-L.; Wang, X.-G.; Hu, B.; Zhang, L.; Zhang, W.; Si, H.-R.; Zhu, Y.; Li, B.; Huang, C.-L.; et al. Discovery of a novel coronavirus associated with the recent pneumonia outbreak in humans and its potential bat origin. Microbiology 2020. [CrossRef]
24. Medical expert group of Tongji hospital. Quick guide to the diagnosis and treatment of pneumonia for novel coronavirus infections (third edition). Herald Med. 2020. http://kns.cnki.net/kcms/detail/42.1293.r.20200130.1803.002.html. Accessed 2 Feb 2020.
25. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. N Engl J Med. 2020. https://doi.org/10.1056/NEJMoa2001316.