

Covid-19 and Gastrointestinal Manifestations in Indian Patients: A Meta-Analysis

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Abstract

Background: India has the second highest number of confirmed Coronavirus cases in the world after the USA with 29.3 million cases reported so far. We aimed to perform a systematic review and meta-analysis of the clinical characteristics, comorbidities, and outcomes of SARS-CoV-2 positive patients with special emphasis on Gastrointestinal (GI) manifestations.

Methods: In this meta-analysis, we conducted a systematic review of high-quality articles on confirmed COVID-19 cases in India published in PubMed and Google Scholar between February 2020 and March 2021. Statistical descriptive analysis and correlation analyses of symptoms, comorbidities and outcomes were performed.

Results: The mean age of the patients was 46.16 years. Of these, 67.53% were males. Overall, 6.4% patients died. Cough (37.79%) was the most common presenting symptom followed by fever (35.5%), nasal congestion, and rhinorrhea (23.60%) but, these symptoms were unrelated to outcome. Patients with shortness of breath ($r = 0.69$, $p = 0.03$) and fatigue/weakness ($r = 0.95$, $p = 0.04$) had high mortality. Hypertension and Diabetes Mellitus were the most common comorbidities but were not associated with negative outcome. Pre-existing chronic kidney disease ($r = 0.80$, $p = 0.01$), mechanical ventilation ($r = 0.895$, $p = 0.003$) and ICU admission ($r = 0.845$, $p = 0.008$) correlated with poor outcome. GI symptoms were reported in 12.05% of the patients. Nausea and vomiting were the most prevalent GI symptoms, but diarrhea ($r = 0.95$, $p = 0.004$) was associated with significant mortality.

Conclusion: Overall, COVID-19 patients in India present with cough, fever, shortness of breath and fatigue as the main symptoms. Among GI symptoms, diarrhea was associated with fatal outcomes. However, more high-quality studies are needed for better understanding of the GI manifestations and their outcomes in the Indian population.

Keywords: Coronavirus Disease-19, Pandemic, Gastrointestinal Manifestation, India

Abbreviations: ACE2: Angiotensin Receptor 2; COVID-19: Coronavirus Disease-19; GI: Gastrointestinal; RT-PCR: Real-time Polymerase Chain Reaction; SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus-2

Introduction

New Coronavirus Disease 2019 (COVID-19) disease emerged in China at the end of 2019 [1]. The Chinese virologists identified a novel virus that was causing flu-like symptoms, and it was named novel Coronavirus (nCoV) on January 12, 2020, by WHO. The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) name was assigned by the International Committee on A Taxonomy of Viruses (ICTV) [2]. India now has the world's second-highest number of COVID-19 cases. Due to its remarkable population density of more than 1.3 billion, along with poor economic conditions and healthcare resources, India is now the epicenter for the COVID-19. As of June 10, 2021, according to the Ministry of Health and Family Welfare (MoHWF). A total of more than 29.6 million confirmed cases and 380,000 Coronavirus-related deaths have been reported in India. Most of the cases have been reported from Maharashtra, Karnataka, Kerala, and Tamil Nadu [3]. India's current COVID-19 surge is an unprecedented public health crisis. With exponential growth in daily COVID-19 cases since March 2021, India reported more than 400,000 new cases daily on May 1, 2021 [4]. This number is likely to be an underestimate of the actual burden of COVID-19 cases, given reports of backlogs of test results, poor access to testing, and many people not getting tested due to fear and stigma [5].

SARS-CoV-2 is unique from other coronavirus infections in that it manifests with multiple extra-pulmonary manifestations. The clinical manifestations of COVID-19 are predominantly respiratory, with cough and shortness of breath being the most prominent presentation. Other prevalent clinical symptoms in patients with COVID-19 include fever and fatigue. The information on extra-pulmonary manifestations, however, has been sparse [6]. Despite being frequently overlooked, Gastrointestinal (GI) tract involvement and the hepatic system are increasingly reported. However, very few studies related to COVID-19 related GI symptoms among the Indian population are available. Increased expression of the Angiotensin Converting Enzyme-2 (ACE-2)

receptor throughout the Gastrointestinal (GI) tract, including gastric, small intestinal and colonic mucosal cells, vascular endothelial cells, cholangiocytes, and smooth muscle cells, are the root cause of GI symptoms and hepatic manifestations [7]. In this study, we aimed to study a comparative analysis of the clinical characteristics, symptoms, and mortality of the confirmed COVID-19 cases reported in India. Particular emphasis was made on GI symptoms and their outcomes.

Methods

Search strategy and selection criteria: We conducted a comprehensive systematic literature search of published articles using electronic databases such as PubMed and Google Scholar and other resources from official health organizations of India such as the Ministry of Health and Family Welfare (MoHFW: <https://www.mohfw.gov.in/>) [3] from February 1st, 2020, to March 31st, 2021. We searched using the following keywords: COVID-19, India, adults, clinical characteristics, GI manifestations, and outcomes. In addition, case characteristics were described, including demographics, exposures, comorbidities, and symptoms. This systematic review and analysis protocol is per the PRISMA-P (Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols) guidance.

Selection and identification of relevant literature: By applying the recorded inclusion and exclusion criteria, we first extracted the Indian COVID-19 studies by title and abstract; then, we compiled the papers by relevance and conducted a new selection process through a comprehensive review of the data. From the selected papers, tables were created for each dataset on Microsoft Excel. These tables included the following information for extracted data of each study: Study author, study period, location, confirmed cases, deaths, lethality rate, median or mean age, sex, fever, shortness of breath, cough, fatigue, myalgia, pneumonia, low oxygenation, loss of appetite, ageusia, anosmia, sore throat, rhinorrhea, abdominal pain, nausea, vomiting, diarrhea, supplemental oxygen, non-invasive ventilation, intubation, hospitalization, ICU transfer, disease severity (asymptomatic, hypertension, cardiac disease, diabetes, obesity, smoking, liver disease, chronic gastrointestinal disease, immunosuppression, cancer, chronic kidney disease, malignancy, dyslipidemia, other comorbidities, positive chest x-ray, laboratory values, administration of Remdesivir, Tocilizumab, Hydroxychloroquine, Ritonavir/Lopinavir, antibiotics.

Inclusion criteria: The following inclusion criteria were considered to substantiate article selection: Confirmed diagnosis of COVID-19 (PCR positive) with at least one gastrointestinal manifestation as reported. No distinction regarding the number of diagnosed cases. There is no distinction regarding sex, age, the severity of disease, inpatient or outpatient management, data collection date, treatment, and outcome.

Exclusion criteria: The following exclusion criteria were adopted to filter out incomplete or ambiguous data: Studies where the cohort was not from India, studies where RT-PCR did not confirm the cases, and studies with incomplete symptoms

or comorbidities report. Papers focusing only on patients who died or had specific comorbidities (i.e., cancer patients, immunosuppressed, hematologic diseases) were excluded.

Statistical analysis: The collected data was used to calculate COVID-19 inpatients from February 1st, 2020- March 31st, 2021. Data collected for each study included the location (study setting) and design, month and year of publication, the total number of patients, comorbidities, symptoms, laboratory findings, treatment, respiratory support, and mortality. The common symptoms and comorbidities were combined and analyzed by weighted analysis methods where relevant. Correlation coefficients were calculated together with regression analysis to establish associations between pre-existing conditions and mortality. The effect of symptoms was reported using weighted analysis where weights were related to the size of the reported study. SPSS (SPSS Inc., Chicago, IL, USA) was used for this analysis.

Results

Adults > 48 years were the most common age group with male preponderance: A total of 5,897 RT-PCR confirmed COVID-19 cases were included in the study. From the confirmed cases we evaluated (Table 1), 67.54% were males and 32.46% were females. The mean age of the study cohort was 46.16 years. There were age differences in this study population of COVID-19 cases. The ages ranged from 35-62 years. Among the 5,897 confirmed cases in this cohort, 33.45% were asymptomatic but still admitted to the hospital quarantine wards during the initial days of the pandemic. All included studies were conducted in in-patient hospital settings.

Cough and fever were the top symptoms, but fatigue and Shortness of breath had severe outcomes: According to combined overall weighted averages, the most common presenting symptoms in the Indian SARS-CoV-2 positive cases were cough with 37.79%, followed by fever with 35.21%. The next common symptoms were nasal congestion and rhinorrhea (23.60%) and shortness of breath with 18.3% (Table 1). While cough and fever were the most common clinical presentations, neither of them was associated with poor outcomes. Presence of shortness of breath ($r = 0.70$, $p = 0.03$) and fatigue/weakness ($r = 0.95$, $p = 0.04$) were associated with mortality.

Diarrhea in COVID-19 Indian cases was associated with poor outcomes: Even though GI manifestations were not commonly reported in many studies, out of 4,994 patients in the study cohort, 12.05% had such symptoms. Among them, the most common presenting symptom was nausea (4.26%), vomiting (4.17%), and diarrhea (3.67%) (Table 1). The presence of diarrhea ($r = 0.915$, $p = 0.004$) was associated with poor outcome.

Diabetes mellitus was the top comorbidity among COVID-19 patients, but the presence of chronic kidney disease was associated with poor outcomes: There were 63.1% of the patients in the study group that were free of any pre-existing conditions. Absence of comorbidities was associated with better outcomes ($r = -0.73$, $p = 0.04$). Among the study

Table 1: Characteristics of Patients in this Study

Study (N = 10)	Mohandas et al. [24]	Mohan et al. [25]	Gupta et al. [26]	Dosi et al. [27]	Sherwal et al. [28]	Goshal et al. [29]	Suresh et al. [30]	Marimuthu et al. [31]	Kayina et al. [32]	Soni et al. [33]	Total
Total Patient Number	3345	144	200	329	308	252	116	854	235	114	5897
% (N)	(56.72)	(2.44)	(3.39)	(5.57)	(5.22)	(4.27)	(1.96)	(14.48)	(3.98)	(1.93)	
Collection date % (N)	April 8 - August 7, 2020	March 2 - April 15, 2020	March 20 - May 8, 2020	March 25 - May 15, 2020	March 17 - May 07, 2020	April - May 2020	May 1 - June 15, 2020	June - September 2020	May 11 - June 28, 2020	April 1 - May 25, 2020	March - September 2020
Age Range	31-65	27-53					39-59	0-90	40-60	13-79	0-90
Female % (N)	30.80 (1031)	7.2 (10)	42 (84)	41.33 (136)	22.4 (69)	19 (48)	37.1 (43)	43.44 (371)	31.91 (75)	42.10 (48)	32.46 (1915)
Male % (N)	69.2 (2314)	93.1 (134)	58 (116)	58.57 (193)	77.6 (239)	81 (204)	62.9 (73)	56.56 (483)	68.1 (160)	57.9 (66)	67.53 (3952)
Asymptomatic % (N = 4692)	28.20 (943)	44.44 (64)	26.5 (53)	45.28 (149)	30.8 (95)	82.5 (208)	-	-	-	50.7 (58)	33.45 (1570)
Fever % (N = 5548)	28.3 (948)	17.4 (25)	54.5 (109)	38.29 (126)	39 (120)	8.3 (21)	59.5 (69)	48.24 (412)	-	-	35.21 (1830)
SOB/ Respiratory syndrome % (N = 5296)	10.4 (348)	5.6 (8)	17.5 (35)	25.83 (85)	12.7 (39)	-	69.8 (81)	29.15 (249)	-	-	18.3 (845)
Nasal Symptoms % (N = 652)	-	21.5 (31)	0.5 (1)	-	9.4 (29)	-	-	-	-	-	23.60 (61)
Cough % (N = 5548)	36.6 (1225)	34.7 (50)	45.5 (91)	32.5 (107)	38.6 (119)	8.3 (21)	63.8 (74)	39.92 (341)	-	-	37.78 (2028)
Fatigue/ Weakness / Malaise % (N = 4070)	5 (116)	1.4 (2)	-	10.63 (35)	-	4.7 (12)	-	-	-	-	5.31 (165)
Myalgia % (N = 5219)	15.4 (515)	3.5 (5)	27 (54)		14 (43)	1.58 (4)	16.4 (19)	21.89 (187)	-	-	15.85 (827)
Pneumonia % (N = 3345)	14.3 (478)	-	-	-	-	-	-	-	-	-	14.3 (478)
Loss of Appetite % (N = 252)	-	-	-	-	-	5.5 (14)	-	-	-	-	5.5 (14)
Loss of Taste (Ageusia) % (N = 3674)	7.4 (248)	-	-	2.43 (8)	-	-	-	-	-	-	6.95 (256)
Loss of Smell (Anosmia) % (N = 4298)	7.4 (248)	-	0.5 (1)	2.43 (8)	1.3 (4)	-	2.6 (3)	-	-	-	6.13 (264)
Headache % (N = 5180)	9.7 (323)	1.4 (2)	11 (22)	2.43 (8)	5.2 (16)	-	-	8.78 (75)	-	-	8.6 (446)
Sore Throat % (N = 5096)	8.6 (289)	21.5 (31)	-	2.43 (8)	13.3 (41)	-	3.4 (4)	8.89 (76)	-	-	8.78 (449)
Chest Pain % (N = 1114)	-	0.7 (1)	-	-	-	-	7.8 (9)	2.92 (25)	-	-	3.12 (35)
GI Symptoms % (N = 502)	15 (502)	-	-	-	-	-	-	-	-	-	12.05 (502)
Abdominal Pain (N = 368)	-	-	0.5 (1)	-	-	2.4 (6)	5.17 (6)	-	-	-	3.53 (368)

Nausea % (N = 396)	-	2.1 (3)	-	-	-	5.5 (14)	-	-	-	-	4.26 (17)
Vomiting % (N = 1149)	-	2.1 (3)	-	3.64 (12)	1.3 (4)	6.34 (16)	11.2 (13)	-	-	-	4.17 (48)
Diarrhea % (N = 2203)	-	2.8 (4)	3 (6)	5.16 (17)	2 (6)	1.1 (3)	8.6 (10)	4.09 (35)	-	-	3.67 (81)
Dyspepsia/ GERD % (N = 329)	-	-	-	0.30 (1)	-	-	-	-	-	-	0.3 (1)
Supplemental Oxygen % (N = 4184)	2.7 (102)	3.5 (5)	-	16.10 (53)	-	3.17 (8)	-	-	-	16.66 (19)	4.5 (187)
Non-Invasive ventilation /CPAP % (N = 955)	-	0.8 (1)	-	14.89 (50)	-	2 (5)	31.03 (36)	-	-	1.75 (2)	10.42 (94)
Intubated % (N)	-	-	-	-	-	-	-	-	18.19 (41)	19.23 (22)	18.02 (349)
ICU Transfer % (N = 4714)	13.20 (441)	3.5 (5)	16 (32)	-	10.7 (33)	-	-	-	-	-	15.6 (511)
Death % (N = 5632)	4.2 (141)	1.4 (2)	8.5 (19)	9.42 (31)	3.6 (11)	2 (5)	51 (50)	10.18 (87)	-	2.63 (3)	6.40 (349)
Low Lymphocyte % (N = 787)	-	6.3 (9)	4.5 (9)	28.57 (94)	-	-	-	-	-	19 (22)	16.7 (134)
High C Reactive Protein % (N = 114)	-	-	-	-	-	-	-	-	-	41 (47)	41 (47)
High Creatinine % (N = 314)	-	2.5 (5)	-	-	-	-	-	-	-	4.2 (5)	3.12 (10)
High AST % (N = 314)	-	10.5 (21)	-	-	-	-	-	-	-	25 (29)	15.64 (50)
High ALT % (N = 314)	-	6.5 (13)	-	-	-	-	-	-	-	32 (36)	15.76 (49)
High D-Dimer % (N = 114)	-	-	-	-	-	-	-	-	-	40.9 (47)	40.9 (47)
High ALP % (N = 114)	-	-	-	-	-	-	-	-	-	29 (33)	29 (33)
Comorbidities At least 1 present (N = 2417)	-	-	41.5(83)	47.11 (155)	-	11.11 (28)	58.6 (68)	29.03 (248)	-	29.9 (34)	36.8 (616)
COPD/ BA % (N = 5260)	0.20 (7)	1.4 (2)	0.5 (1)	-	-	1.2 (3)	2.6 (3)	1.52 (13)	2.12 (5)	1.75 (2)	0.8 (36)
Asthma % (N = 4459)	2.9 (98)	0.7 (1)	-	-	-	-	4.3 (5)	1.40 (12)	-	-	2.56 (116)
Hypertension % (N = 5598)	29.1 (974)	2.1 (3)	23 (46)	24.92 (82)	-	1.2 (3)	30.2 (35)	23.18 (198)	27.6 (65)	16.6 (19)	25.5 (1425)
Cardiac disease % (N = 5337)	6 (200)	0.7 (1)	4.5 (9)	3.94 (13)	-	-	6.9 (8)	4.33 (37)	5.53 (13)	1.75 (2)	5.33 (283)
Metabolic, Diabetes % (N = 5598)	37.1 (1240)	11.1 (16)	16 (32)	21.58 (71)	-	2.38 (6)	27.6 (32)	23.41 (200)	22.9 (54)	14.9 (17)	29.8 (1668)
Obesity % (N = 443)	-	-	-	1.21 (4)	-	-	-	-	-	0.88 (1)	1.13 (5)
Smoking % (N = 1250)	-	6.25 (9)	-	-	-	4.36 (11)	-	1.17 (10)	-	-	2.42 (30)
H/O Liver disease % (N = 465)	-	-	-	-	-	-	6.9 (8)	-	4.25 (10)	0.87 (1)	4.11 (19)
Chronic Kidney Disease % (N = 5445)	1.6 (52)	-	2 (4)	1.82 (6)	-	5.5 (14)	15.5 (18)	1.17 (10)	9.36 (22)	2.63 (3)	2.04 (129)

Malignancy % (N = 1986)	-	-	2.5 (5)	0.60 (2)	-	0.4 (1)	8.65 (10)	1.17 (10)	11.0 (26)	-	2.72 (54)
Thyroid disorder % (N = 4986)	2.8 (94)	2.1 (3)	3 (6)	3 (10)	-	-	-	5.26 (45)	-	5.26 (6)	3.28 (164)
Tuberculosis (TB) % (N = 1054)	-	-	5.5 (11)	-	-	-	-	1.17 (10)	-	-	2.05 (21)
Tocilizumab % (N = 3459)	6.9 (231)	-	-	-	-	-	-	-	-	1.75 (2)	6.73 (233)
Hydroxychloroquine / Chloroquine % (N = 3603)	11.5 (384)	18.7 (27)	-	-	-	-	-	-	-	32.4 (37)	16.7 (448)
Antibiotics % (N = 3603)	100 (3345)	20.1 (29)	-	-	-	-	-	-	-	7.89 (9)	89.9 (3383)
LMWH (N = 3345)	48.6 (1626)	-	-	-	-	-	-	-	-	-	48.6 (1626)
Steroids (N = 3345)	53.5 (1789)	-	-	-	-	-	-	-	-	-	53.5 (1789)

cohort, we analyzed 36.87% of the patients who had at least one comorbidity. Diabetes mellitus (29.8%) was the most common pre-existing disease followed by hypertension (25.5%). Patients with chronic kidney disease were associated with increased mortality ($r = 0.80$, $p = 0.01$).

Elevated liver function tests, low lymphocyte count were the most altered laboratory markers: Among the laboratory tests, 17% of the patients had low lymphocyte count (Table 1). ALP (29%), AST (15.7%), and ALT (15.7%) were elevated in the study cohort. But elevated liver enzymes and low lymphocytes count were not associated with poor outcomes. The widely used treatment options for COVID-19 patients were antibiotics (90%) such as azithromycin and beta-lactams, followed by Hydroxychloroquine (16.7%).

Mechanical ventilation and ICU admission patients were prone to poor outcome: Overall, 10.42% of the patients received mechanical ventilation ($r = 0.89$, $p = 0.003$). Its use associated with poor prognosis among hospital admitted COVID-19 patients. A total of 15.6% of the patients were admitted to the ICU ($r = 0.84$, $p = 0.008$) and had poor outcomes. The mortality rate among the study cohort was 6.4%. The most used treatment options in the inpatient hospital setting in India were antibiotics (89.9%), steroids (53.5%), and Low Molecular Weight Heparin (LMWH) (48.6%).

Discussion

India's COVID-19 confirmed cases topped more than 29 million, which is now ranked second for the total number of Coronavirus cases after the US. The increasing spread of the SAR CoV-2 remains a public health emergency of international concern. As with other countries globally, India too started vaccination campaigns in January 2021; simultaneously, reports of Variants of Concern (VOCs) were communicated from the UK, Brazil, and South Africa. In this systematic review and meta-analysis of including ten studies with 5,897 patients, we assessed

clinical characteristics, risk factors with particular emphasis on GI manifestation in the COVID-19 confirmed cases in India. The data suggest that the hospitalized patients for COVID-19 in India were younger (median age 46.3 years) compared to the USA and European cases (median ages 68 and 63 years, respectively) with less proportion of comorbid condition (36.3%) compared to the western countries (75%) [8-10]. As mentioned in previous studies, diabetes mellitus and hypertension were the most prevalent comorbidities in COVID-19 cases in India [11,12]. However, they did not associate with poor outcomes. The presence of pre-existing chronic kidney disease was a predictor of poor outcome in correlation analysis, consistent with Pakhchanian, et al. study [13].

In our study, 12% of the patients had GI manifestations. The GI and liver manifestations of COVID-19 and their outcomes have been described in multiple studies across the world, but very few studies are done so far in India. Evidence of GI infection by SARS-CoV-2 has also been provided by isolating viral RNA from GI epithelial cells and intracellular staining of viral nucleocapsid protein in intestinal tissues. Higher co-expression of ACE2 and TMPRSS2 and more robust binding efficiency of SARS-CoV-2 for ACE2, located on the mature enterocytes in the ileum and colon, triggers epithelial cell fusion TMPRSS2 and TMPRSS4 suggesting the viral invasion of enterocytes of the digestive tract and stratified epithelial cells of the esophagus [14]. Based on this, it is hypothesized that SARS-CoV-2 infection of intestinal enterocytes causes dysfunction of the ileum and colon, subsequently leading to various GI manifestations seen in COVID-19 patients. The GI symptoms included in our analysis were nausea, vomiting, diarrhea, abdominal pain, and anorexia which is consistency with Luo S, et al. and Wei, et al. studies [15,16].

Among the reported GI symptoms, diarrhea was associated with poor outcomes in this study. Jin, et al. reported that gastrointestinal symptoms in adults were associated with more severe illness and worst prognosis [17]. It is noteworthy

that as much as 53.4% of patients had detectable viral nucleic acids in their stool samples in study conducted, suggesting that SARS-CoV-2 might directly damage the intestinal mucosa, causing digestive disturbances [18]. Patients with COVID-19-associated diarrhea are vulnerable to dysbiosis of the intestinal flora, resulting in severe illness. The high-risk score of critically ill COVID-19 patients was positively correlated with pro-inflammatory factors closely related to the human intestinal flora [18]. Diarrhea in COVID-19 cases disrupts the intestinal flora, affects the inflammatory response, increases the severity of COVID-19, and is associated with the worst prognosis [19]. Most patients with COVID-19 were administered broad-spectrum antibiotics and antiviral drugs, which could cause drug-related diarrhea during hospitalization. In cases of diarrhea after admission, drug-related diarrhea should be excluded to determine the true incidence of COVID-19-associated diarrhea. Emphasis on observing the GI and liver manifestations is required among the Indian population. Monitoring viral RNA in fecal specimens might benefit disease prediction and surveillance. The presence of gastrointestinal signs and symptoms of COVID-19 could be used to predict whether patients would develop severe respiratory disorders, which will help to design more beneficial treatment plans for patients.

The laboratory tests are important markers of underlying causal factors of observed clinical manifestations and prognosis. Indeed, 16.7% of patients displayed low lymphocytes count that was not associated with poor prognosis. This contrasts with Illg, et al. study, demonstrating that the degree of lymphopenia correlates with COVID-19 severity [14]. The low lymphocyte count could be due to the injudicious use of glucocorticoids. Liver dysfunction may be common in patients with severe COVID-19 infections. Though primarily a respiratory pathogen, shreds of evidence indicate the liver as an extra-pulmonary site for SARS-CoV-2 infection, causing liver injury ranging between 14.8% to 78% [15,20]. The possible mechanism of hepatic injury in COVID-19 could either be a virus-related cytopathic effect or an infection-induced cytokine storm. In this study, ALT, AST and ALP were elevated in 15.76%, 15.75%, and 29%, respectively. In their study in India, Koushik, et al [21]. mentioned that the prevalence of abnormal liver function tests in patients of COVID-19 is 59.04%. Elevated Liver enzymes were not associated with poor outcomes in our study, supported by the study conducted by Wang, et al [22]. But, this contrasts with the Asghar, et al study results stating correlation between elevated LFTs and increased mortality [23]. This could be because some of the patients were still under treatment or hospitalized at the time of publication, and the outcome of these patients was not measured. The use of antivirals might also be the reason for the elevated LFTs leading to the drug-induced liver injury. More prospective studies collaborating data of LFTs, viral load of SARS-CoV-2, and Liver histology for Drug-related liver injury in the COVID -19 patients help us better understand these patients' outcomes. This meta-analysis also highlights that the number of patients requiring supplemental oxygen was low (8.3%). However, the proportion of patients requiring mechanical ventilation were comparatively high, and this contrasts with the studies done by De Souza, et al.

and will need further investigations [12].

In conclusion, with the COVID-19 pandemic still fuming with new variants, scarcity of vaccines in India, and overwhelming burden on the healthcare system, the only interventions that can help curb the spread of the virus are modifying human behavior measures as social distancing, hygiene, and wearing masks. This should limit the exposure and break the transmission chain. There might be differences in the socioeconomic strata of the patients admitted to hospitals other than those mentioned in our analysis. Studies in our analysis did not report the cultural, healthcare access, government policy, and socioeconomic variables which might have altered the outcomes in the patients. Extensive prospective studies will be required to fully understand the difference in cultural and socioeconomic differences associated with the development and progression of COVID-19 infection in India.

Author Contributions

Study concept and design (HA), Data acquisition (LG, AP), Data analysis and interpretation (HA, HB, LG, AP), Drafting of manuscript (HA, HB, LG), Statistical analysis (GO), Obtained funding (HA), Material support (LG). All Authors read and approved the manuscript.

Ethics approval and consent to participate: The de-identified data in this study does not need consent form since it is available in the published articles or from the ministry of health of country of interest. All resources have been cited in the paper.

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Competing Interests

No potential conflicts of interest are disclosed.

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