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Original Research Article

Surgical outcome of COVID-19 infected patients: experience in a tertiary care hospital in India

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ABSTRACT

Background: COVID-19 disease caused by SARS-COV-2 has become a pandemic. Outcome of surgical patients infected with COVID-19 is not very clear.
Methods: Retrospective analysis of the surgical outcome of COVID-19 infected patients admitted in emergency and elective surgical settings in a designated COVID care center.
Results: Total 53 patients were included. Surgery was done in 47.16% (n=25) patients and 52.84% (n=28) patients were managed non-operatively. Overall mortality was 37.7 % (n=20). In operated group it was 52% (n=13) and 25% (n=7) in the non-operative group (p=0.043). The total leukocyte (p=0.018), serum CRP (p=0.031), urea and creatinine level (p=0.025) were higher in the mortality group. Patients aged more than 50 years had a significantly higher mortality compared to less than 50 years (p=0.010). Patients having multiple comorbidities had higher mortality (p=0.159).
Conclusions: COVID-19 infection has a definite adverse impact on the outcomes of surgical patients.

Keywords: COVID-19, COVID-19 infection in surgical patients, COVID-19 pandemic and surgical outcome

INTRODUCTION

Coronavirus Disease 2019 (COVID-19), an infectious disease caused by severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) had quickly become a global burden and was declared as a pandemic by World Health Organization (WHO) on 11th March 2020.[1] The first case of COVID-19 in India was diagnosed on 30th January 2020. The initial spread was limited as a result of the lockdown, but the numbers rose exponentially as the restrictions were relaxed.[2] India is one of the worst affected countries with over 6 million cases at the time of this study.[3] COVID-19 has dramatically affected the already overburdened Indian healthcare facilities. Surgical care in the current pandemic presents a unique challenge as the merits of carrying out elective and semi-elective surgeries for the patient's benefit has to be balanced against the increased risk of acquiring the infection by the patients, their attendants as well as the healthcare providers. Emergency surgical management poses further questions about the optimum use of personal protective equipments (PPE) and change in management strategies, all while putting the patient's interest at the forefront. Several professional bodies have recommended a higher threshold for operative management in view of poor outcome in surgical patients.[4,5] With each passing day, more and more information is being made available regarding the

characteristics of the disease and its behavior. There is a need to study the outcome of these patients and redefine the management protocols and fill the lacunae. This study aims to study the outcome of surgical patients infected with COVID-19 in one of the tertiary care center in northern India.

METHODS

We retrospectively analyzed the data of 53 COVID-19 infected surgical patients who presented in the Department of General Surgery during the study period from May 2020 to October 2020. The main objective of the study was to find out the outcome of surgical patients infected with COVID-19 infection in terms of mortality. The diagnosis of COVID-19 was done by RT-PCR methods using nasopharyngeal swab. Patients aged between 19 years and 80 years of age were included in the study. Institutional Ethical Committee clearance was taken and informed consent was taken from patients as per protocol. Once diagnosed to be COVID-19 positive, all patients were treated as per international COVID-19 guidelines. Patients who were diagnosed to be COVID-19 positive before surgery were operated in a designated COVID block of the hospital with standard PPE as per institutional protocol. Patients were followed up for a period of one month and 30-day mortality was recorded. Subgroup analysis was carried out based on age, sex, biochemical parameters, mode of management, timing of surgery, comorbidities and outcome in emergency and elective settings.

Statistical analysis was carried out using IBM SPSS Version 26. Continuous data were tested for distribution; normally distributed data was analyzed using mean with standard deviation (SD) and 95% CI (confidence interval) and skewed data analyzed using median. Differences between the two groups were tested using the unpaired t-test. ANOVA and Student's t-test were used for continuous quantitative data analysis in subgroups. The χ^2 and Fisher's exact tests were used for categorical data. Multi-level logistic regression was used to calculate odds ratios (ORs) and 95% CIs. Models included factors that occurred before the outcome of interest.

RESULTS

Total of 53 patients were included in the study. Twenty-five patients were operated and 28 patients underwent non-operative management. In the operated group, 15 patients were diagnosed with COVID-19 before surgery, whereas 10 patients were diagnosed with the COVID-19 infection in the post-operative period. The mortality was 37.7% (n=20); 13 in the operative group and 7 in non-operative group (p=0.043 (CI 1.02 -10.38) OR=3.25) (Table 1).

Table 1: Demographic and biochemical parameters comparison between non-operative and operative groups.

Characteristics	Number of patients (n=53) mean (SD)	Non- operative group (n=28) mean (SD)	Operative group (n=25) mean (SD)	P value
Age (years)	47.6 (17.7)	49.6 (15.5)	45.5 (20.0)	0.24
Man: Woman	31:22	15:13	16:9	0.442
Mortality	20	7	13	0.043
Hemoglobin (g/dl)	10.1 (2.3)	10.2 (2.1)	9.9 (2.5)	0.739
TLC (10^6/l)	10770 (5559)	9726 (4369)	11940 (6541)	0.045
N/L ratio	8.4 (9.5)	6.54 (4.6)	10.51 (12.8)	0.061
Prothrombin (sec)	20.5 (11.4)	17.0 (4.1)	24.4 (15.3)	0.018
APTT (sec)	32.9 (7.4)	32.3 (7.8)	33.5 (6.9)	0.688
INR	1.42 (0.7)	1.2 (0.2)	1.6 (0.9)	0.017
D-dimer (µg/ml)	1888 (2242)	1073 (1337)	2407 (2591)	0.344
Ferritin (ng/ml)	327.7 (346)	22 (15)	378 (349)	0.388
Fibrinogen (g/l)	5.1 (2.1)	4.4 (1.4)	5.7 (2.5)	0.184
CRP (mg/l)	102 (98.7)	63.5(47.8)	181.5 (152.7)	0.192
LDH (U/l)	360.6 (142.1)	342.2 (155.8)	373.8 (142.6)	0.903
Bilirubin*	0.8	0.75	0.8	0.163
SGOT*(U/l)	43	39.7	55.4	0.291
SGPT*(U/l)	35	37	29	0.721
ALP*(U/l)	87	95.5	78	0.166
sodium (meq/l)	137.6 (6.0)	135.9 (6.3)	139.5 (5.1)	0.545
potassium (meq/l)	4.2 (0.6)	4.2(0.5)	4.2 (0.6)	0.199
urea (mg/dl)	37.5 (28.0)	37.3 (26.4)	37.7 (30.5)	0.767
creatinine (mg/dl)	1.0 (0.9)	1.05 (1.0)	0.87 (0.7)	0.429
calcium (mg/dl)	7.6 (1.6)	8.3 (0.9)	7.0 (1.7)	0.143
magnesium (mg/dl)	1.9 (0.3)	2.0 (0.3)	1.9 (0.3)	0.890

*Median value.

Table 2: Diagnosis and mortality analysis.

Diagnosis	Total patients n=53	Total deaths n=20	P value
Emergency			
Perforation	10	6	
Vascular	9	3	
Trauma	7	2	
Obstruction	4	3	0.003
NSTI	3	3	(odd ratio 9.56; CI 1.90-47.96)
Bowel Gangrene	1	1	
Elective			
Benign	7	1	
Malignancy	12	1	
Cause of death			
Multiorgan dysfunction syndrome (MODS) n=8 (40%)			
Acute respiratory distress syndrome (ARDS) n=6 (30%)			
Sudden cardiac death n=6 (30%)			
Pulmonary embolism			
Acute coronary syndrome			
Arrhythmias			

Table 3: Comparison between the survivors and mortality group.

Characteristics	Overall patients (n=53) mean (SD)	Mortality (n=20) mean (SD)	Survivor (n=33) mean (SD)	P value
Age (years)	47.6 (17.7)	55.6 (15.6)	42.2 (16.8)	0.267
Man : Woman	31: 22	12 : 8	19:14	0.862
Hemoglobin (g/dl)	10.1 (2.3)	9.7 (2.4)	10.3 (2.2)	0.714
TLC (106/l)	10770 (5559)	13360 (6490)	9201 (4299)	0.018
N/L ratio	8.4 (9.5)	13.0 (13.1)	5.6 (4.8)	0.068
Prothombin time (sec)	20.5 (11.4)	20.4 (5.6)	20.6 (13.9)	0.270
aPTT (sec)	32.9 (7.4)	35.8 (8.3)	31.2 (6.3)	0.052
INR	1.4 (0.7)	1.4 (0.4)	1.4 (0.8)	0.270
D-dimer (µg/ml)	1888 (2242)	2712 (3143)	1364 (1357)	0.214
Ferritin (ng/ml)	328 (346)	482 (27)	266 (403)	0.217
Fibrinogen (g/l)	5.1 (2.1)	4.6 (2.1)	5.5 (2.0)	0.891
CRP (mg/l)	102.8 (98.7)	92.6 (20.2)	113.1 (153.8)	0.031
LDH (U/l)	360 (142)	420 (139)	318 (138)	0.994
Total Bilirubin* (mg/dl)	0.8	0.8	0.79	0.229
SGOT* (U/l)	43	64.8	36.6	0.181
SGPT* (U/l)	35	33.8	35	0.392
ALP* (U/l)	87	102.5	84.5	0.684
Sodium (meq/l)	137.6 (6.0)	139.4 (7.7)	136.5 (4.5)	0.032
Potassium(meq/l)	4.2 (0.6)	4.3 (0.8)	4.1 (0.4)	0.005
Urea (mg/dl)	37.5 (28.1)	54.3 (36.5)	27.3 (14.6)	<0.0005
Creatinine (mg/dl)	1.0 (0.9)	1.3 (1.3)	0.8 (0.3)	0.025
Calcium (mg/dl)	7.6 (1.6)	6.9 (2.1)	8.2 (0.7)	0.074
Magnesium (mg/dl)	1.9 (0.3)	1.8 (0.3)	2.0 (0.2)	0.164

*Median value

Mortality was higher in patients admitted in emergency 52.9%, as compared to patients admitted for elective surgery 10.5% (p=0.003 OR 9.56 CI 1.90-47.96) (Table 2). There was no difference in the mortality between the two groups in terms of COVID positive or COVID negative status at the time of surgery (p=0.688 (CI 0.34–8.68)). The indications for surgery in emergency patients were bowel perforations followed by vascular and trauma cases, bowel obstruction, necrotizing soft tissue infection and bowel gangrene (Table 2).

The total leukocyte were counts and Neutrophil and Lymphocyte ratio was higher in the mortality group (13360 vs. 9201; p=0.018), (13 vs. 5.6; p=0.068) respectively. Serum urea, creatinine and CRP level were also higher in mortality group (p=0.025 and p=0.031 respectivly) (Table 3). Rest of the parameters like hemoglobin, bilirubin, aspartate transaminase, alanine transaminase, alkaline phosphatase, prothrombin time, activated partial thromboplastin time; INR, D-dimer, ferritin, fibrinogen and LDH were not significantly different in the two groups (Table 3). Age more than 50 years had higher mortality (55.6%) in comparison to less than 50 years (19.2%), which was statistically significant ((p=0.010) CI 1.53-18.07; OR=5.25).

Patients with comorbidities had worse outcome. Mortality was more common in patients having comorbidities (46.7%) compared to non-comorbidities group (26%) (p=0.159, odd ratio 2.48). Individual comorbidities reveal a statistically significant increase in mortality in diabetics (7/9) (p=0.019, (CI1.52-45.67); OR=8.35) and hypertensive (8/10) (p=0.004, (CI=1.91-55.82); OR=10.33).

There was 30% (n=6) mortality that were directly associated with COVID-19 related pulmonary complications like pneumonia and ARDS. Total 40% (n=8) patients develop multi organ dysfunction syndrome and sepsis while 30% (n=6) patients had sudden death without any precipitating events.

During the follow up period, 3 patients developed symptoms after discharge from hospital, 1 patient died during the course of readmission due to sudden onset dyspnea while 2 patients required readmission following initial discharge (one died in the hospital).

DISCUSSION

The current pandemic has posed a unique challenge to surgeons and their patients. Several studies have shown a higher incidence of pulmonary complications and mortality in surgical patients suffering from SARS COV-2 infection. An international, multicenter, cohorts study at 235 hospitals in 24 countries, reported pulmonary complications in 51.2% of patients and a 30-day mortality of 38.0%.[4] A Dutch multicenter matched cohort study yielded similar results- pulmonary complications were noted in 51% of patients and a mortality rate of 28%.[5] In our study total 25 patients were operated while 28 patients were managed non-operatively. Thirteen patients died in the operative group while 7 patients died in the non-operative group. The reasons underlying the increased mortality rate of COVID-19 positive patients undergoing surgery are not well known. Mechanical ventilation, anesthesia or tissue damage caused by surgical stress may each provoke a pro-inflammatory and immunosuppressive response, potentially worsening the condition of a pre or postoperative COVID-19 infected patients.[5] Consequentially, it is advisable to delay surgical intervention whenever feasible.[6] It was also observed that timing of surgery in COVID-19 patients did not alter the outcome in terms of mortality and surgery was an independent risk factor for adverse outcome - a finding consistent with other study.[4]

Patients with co-morbidities, especially diabetes mellitus and hypertension were particularly at higher risk of adverse outcomes. An international cohort study by COVID Surg Collaborative revealed that in adjusted analyses, having ASA grades 3-5 versus ASA grades 1-2 was associated with increased odds of 7 days mortality (OR 2.52 (95% CI 1.10-5.77)).[4] Our study also revealed a higher mortality rate in diabetics and hypertensive patients. The association of other comorbidities with adverse outcomes could not be replicated in our study possibly due to a small sample size.

In several studies, higher mortality was noted in patients aged more than 70 years.[4,5] We found an increased mortality in the group of patients aged >50 years. This could be due to lower median age in Indian population and large proportion of population in the young age group. This could have definite implications for India in terms of identifying at-risk group of patients where mean age is less than 30 years.[7]

The particularly high incidence of cardiac cause of death (30% deaths in our study) needs further elaboration as they occurred in the absence of any precipitating event. This could be attributed to pulmonary thromboembolism, acute coronary syndrome or arrhythmias considering the hypercoagulable state due to widespread endothelial injury aggravated by COVID-19 infection. Whether COVID-19 infection predisposes a patient to major adverse cardiac events or not remains to be seen. Studies have shown to increase risk of pulmonary complications, increased risk of sepsis and organ failures, which increases morbidity and mortality in COVID-19 patients.[8]

The effect of pro-inflammatory markers like CRP, Procalcitonin, fibrinogen, ferritin and ESR on predicting outcome of COVID-19 patients has come under intense scrutiny, with some studies suggesting that the level of these markers can be used to predict the severity of the disease while others did not find any significant correlation between the two.[9,10] We did not find a significant correlation between the two; except raised TLC, N/L ratio, serum CRP, urea and creatinine. Further large-scale studies are required to study the association.

Limitations

This study has several limitations. The sample size is small and the group is heterogeneous - including patients in emergency as well as elective setting and with varied diagnoses. The follow up period was limited and only early outcomes could be investigated. Subgroup analysis could not be carried out in all groups.

CONCLUSION

In conclusion, co-infection with COVID-19 virus predisposes surgical patients to adverse outcomes. Patients aged more than 50 years, having co-morbidities, presenting with surgical emergencies or patients who undergo surgical intervention are at a particularly higher risk. It is thus recommended to opt for non-operative management whenever feasible. The effect of pro-inflammatory markers on predicting the outcome requires further investigation. The cause of death in this subgroup of patients also requires elaboration to ascertain where these patients are predisposed to major adverse cardiac events due to hypercoagulable state or arrhythmias.

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