

A Case Series of Amoebic Liver Abscess in Patients With COVID-19 Infection



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Background: Globally, amoebiasis is the second leading cause of death due to parasitic diseases. Amoebic liver abscess (ALA) as an opportunistic infection in recently recovered COVID 19 disease patients has not been reported earlier. **Methods:** We present here a case series of 13 patients of ALA admitted during the month of May 2021 in BLK hospital, New Delhi, and had recently recovered from COVID 19 disease. **Results:** Out of 13, eight patients had moderate, and one had severe COVID 19 disease. All these patients had received steroids for the management of COVID 19 disease. The remaining 4 (30%) patients had mild disease. The mean age of our patients was 50 years (37–81 years). Out of 13 patients, nine (70%) were male, 5 were diabetic, 2 were hypertensive, and none were alcoholic. The most common presentation was fever (11/13) followed by upper abdomen pain (10/13). The mean time of symptom (fever or pain abdomen) onset from COVID 19 positivity date was 19 days (range 15–23 days). A complication in the form of localized intraperitoneal rupture was common in these patients and was seen in more than 50% (7/13) of patients. All the patients were managed with IV Metronidazole and abscess aspiration. All the patients were discharged, and the mean hospital stay was 6.6 days. **Conclusion:** We report here an increase in the incidence of ALA in recently recovered COVID 19 patients and propose that it is most likely due to alteration in the immune state of these patients. It is important for physicians to investigate for liver abscess in patients who present again with fever and/or pain abdomen within 2 weeks of COVID 19 recovery. (J CLIN EXP HEPATOL 2022;12:1017–1020)

Amoebiasis is the second leading cause of death due to parasitic diseases, leading to deaths of about 40,000–100,000 people per year globally.¹ It is endemic in the Indian subcontinent. *Entamoeba histolytica* has a 2-stage life cycle that consists of an infectious cystic and a motile trophozoite stage.² The infection occurs via the fecal-oral route through ingestion of cyst. Excystation occurs in the small intestine, resulting in the release of trophozoites and colonization of the terminal ileum/caecum area. In 90% of infected patients, trophozoites are encysted and passed in stools, other 10% penetrate and invade the colonic mucosal barrier, leading to tissue destruction and secretory bloody diarrhea. In addition, trophozoites can spread hematogenously via portal circulation to the liver or even to more distant organs. Amoebic liver abscess is the most common extraintestinal manifestation of this protozoan.²

The ongoing pandemic of COVID 19 disease has affected more than 170 million people all over the world.³ Also it is now known that secondary bacterial and other

viral infections lead to recurrent admissions, increased morbidity, and mortality of affected patients.⁴

The second wave of COVID 19 disease in India was much larger than the first, and the daily count on April 15, 2021, itself was double that of the first peak. The new virus strain Delta is more infective and leads to an increase in the number of moderate to severe COVID 19 disease.

Although India continues to achieve stability over the existing situation, the reported incidence of fungal infections has increased in patients who recovered from COVID 19 disease.⁵

We noticed an increase in the number of patients with an amoebic liver abscess admitted in our hospital in the month of May 2021. We planned a retrospective analysis of these patients admitted with us during this period.

METHODS

We analyzed the hospital admission records for all patients admitted with a diagnosis of Amoebic Liver Abscess (ALA) in departments of Gastroenterology, Internal medicine, Pulmonology, and Critical care at BLK Hospital, New Delhi, during the month of May 2021. In total, 16 patients were diagnosed and admitted for ALA in May 2021. To see if the admissions have actually increased in the COVID peak era, we also reviewed our hospital records for the number of admissions of patients with an amoebic liver abscess in the last six months, i.e., November 2020–April 2021. Also, in view of seasonal incidence of ALA, we

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Abbreviations: ALA: Amoebic liver Abscess; COVID 19: 2019 novel coronavirus

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Table 1 Demographic and Clinical Profiles of 13 Cases of Amoebic Liver Abscesses in Recently Recovered COVID 19.

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8	Patient 9	Patient 10	Patient 11	Patient 12	Patient 13
SEX	M	F	F	M	M	M	M	M	M	F	M	F	M
AGE	41	53	38	81	51	46	47	55	39	68	41	37	64
CT SEVERITY	Moderate	Moderate	Moderate	Mild	Mild	Mild	Severe	Mild	Moderate	Moderate	Moderate	Moderate	Moderate
STEROIDS RECIEVED	Yes	Yes	Yes	No	No	No	Yes	No	Yes	Yes	Yes	Yes	Yes
DAYOF PRESENTATION FROM COVID POSITIVE	16	18	17	15	21	20	19	23	20	18	18	21	24
DM	Yes	Yes	No	No	No	No	Yes	Yes	No	Yes	No	No	No
COMORBIDITIES	nil	HTN	nil	nil	nil	nil	nil	nil	nil	HTN	nil	nil	nil
CHRONIC ALCOHOL	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO
MULTIPLE LIVER ABCESS	Yes	Yes	Yes	Yes	No	No	No	No	No	No	No	No	No
VOLUME IN CC	74	178	400	70	155	60	200	290	137	90	200	100	106
ABSCESS ASPIRATION	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES
AMOEBIC SEROLOGY	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive
CAECAL INVOLMENT	No	Yes	No	No	Yes	No	No	No	No	No	No	No	Yes
OUTCOME	Discharge	Discharge	Discharge	Discharge	Discharge	Discharge	Discharge	Discharge	Discharge	Discharge	Discharge	Discharge	Discharge
DURATION OF HOSPITAL STAY (days)	6	8	5	7	4	6	5	6	14	5	4	8	8

recovered the data of all ALA admissions in the month of May 2020 to compare with the number of admissions last year during the same time period. The total number of admissions of patients with amoebic liver abscess was three in the month of May 2020, 24 during November 2020–April 2021, and 16 in the month of May 2021. Thirteen out of these 16 patients of amoebic liver abscess diagnosed in the month of May 2021 had recently recovered from COVID 19 disease. The total number of COVID 19 disease-related admissions in our hospital was 550 in the month of May 2021.

The diagnosis of the amoebic liver abscess was made if there was imaging ultrasonography or CT triple-phase showing (a) findings suggestive of liver abscess (b) Positive Amoebic serology IgG-Elisa >11.0 U and/or (c) Anchovy sauce appearance on abscess aspiration, (d) If an abscess was aspirated, negative pus culture.

We present the case series of these 13 patients with an amoebic liver abscess who recently recovered from COVID19 disease.

RESULTS

The demographic, clinical, serological, and imaging profiles of these 13 patients were recorded (Table 1). Out of 13 patients, 8 had moderate, and 1 patient had severe COVID 19 disease. All patients with moderate and severe disease (9 out of 13) received steroids for management of COVID19 pneumonia. None of the patients received tocilizumab for the management of COVID-19. Four patients had mild infections and were managed as outpatients. None of the patients with mild disease received steroids.

All the patients had imaging evidence of liver abscess on USG abdomen and/or CT triple-phase abdomen with positive amoebic serology and negative pus cultures from the abscess aspirate. The mean age of our patients was 50 years (37–81 years). Out of 13 patients, nine (70%) were male, 5 were diabetic, 2 were hypertensive, and none were alco-

holic. The most common presentation was fever (11/13) followed by pain upper abdomen (10/13). Two patients were incidentally detected to have liver abscess on a USG of the abdomen; out of these two, one had an unexplained rise in the total leucocyte count, and the other patient presented with altered stool color. The mean time of symptom (fever or pain abdomen) onset from COVID 19 positivity date was 19 days (range 15–23 days).

The size of liver abscesses varied from the largest being 400 cc and the smallest 60 cc respectively. Nine out of 13 patients had a solitary liver abscess, and of whom five had left lobe liver abscess.

A complication in the form of localized intraperitoneal rupture was common in these patients and was seen in 7 out of 13 patients. Four of these seven patients had solitary left lobe abscesses, and the rest three had bilobar abscesses (Figure 1). Cecal involvement in the CT triple-phase abdomen was seen in three patients.

All the patients were treated with IV metronidazole and USG guided liver abscess aspiration. In seven patients with complicated liver abscess, percutaneous catheter drainage was done, and in the rest six, single-time aspiration. All the patients recovered and were discharged from the hospital. Mean hospital stay was 6.6 days (range 5–14 days).

DISCUSSION

Our case series highlights the possibility of a correlation between COVID-19 and amoebic liver abscess. The number of patients admitted for ALA was much higher in May 2021 compared to the previous 6 months, as well as in May 2020. Most of these patients (13 of 16) had recently recovered from COVID infection, thus raising a suspicion that COVID 19 predisposes to the development of ALA. Four out of 13 patients had mild COVID19 disease (and did not receive steroids); the other nine had received steroids for COVID 19 related complications. We postulate that the predisposition to develop ALA may be related to

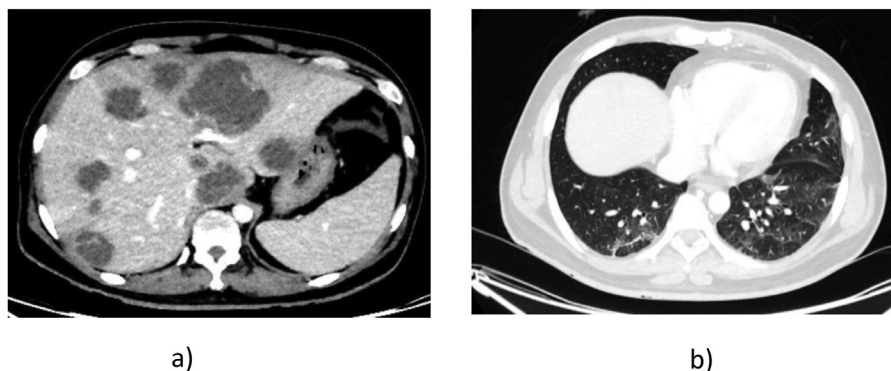


Figure 1 a) Contrast-enhanced CT abdomen of one of the patients showing multiple scattered hypodense lesions in both lobes of the liver with a peripheral rim of edema consistent with multiple liver abscesses. (b) Sections of chest CT of the same patient shows few ground glass densities with curvilinear bands in bilateral lower lobes.

COVID 19 itself and may be accentuated by the use of steroids. The complication rate in these patients was also observed to be higher (more than 50% presented with localized rupture). This may be attributable to the steroid use (due to COVID 19), which may have masked the initial symptoms leading to late presentation.

Both innate and cell-mediated immunity plays a significant role in the pathogenesis of amoebic liver abscess. The risk factors for amoebic liver abscess are alcoholism, male sex with age 18–50 years, malnourishment, thymectomy and splenectomy, diabetics, corticosteroid use, and altered cell-mediated immunity like HIV infection.^{6,7}

Recent data suggest that COVID 19 disease leads to suppression of cell-mediated and innate immunity. SARS COV2 infection is associated with lymphopenia in moderate and severe cases. In recent studies, the counts of CD8⁺ T, memory CD4⁺ T cells, and Treg cells were shown to be decreased.⁸

In addition, functional exhaustion of T cells has been reported in COVID-19 patients as indicated by upregulation of exhaustion markers, including PD-1, CTLA-4, TIGIT, and TIM-3 and downregulation of IFN- γ , TNF- α , granzyme B, and IL-2.⁹

The recent randomized control trial reported a decrease in mortality of patients of COVID 19 disease who were on oxygen support with the use of dexamethasone.¹⁰ Glucocorticosteroid leads to peripheral neutrophilia, inhibits the release of cytokines and chemokines, and impairs leucocyte migration site of inflammation. It also leads to lymphopenia (T cells more than B cells). This may have contributed to the higher complication rate in the patients developing ALA in our cohort.

Both SARS-COV2 infection and the use of glucocorticoids lead to suppression of the immune system. This immunosuppressed state may lead to opportunistic infections in patients with COVID19 disease. Treating clinicians need to be aware of the possibility of these infections and should rationalize the use of corticosteroids. The first four weeks from the date of COVID 19 positivity are important, as all the patients with amoebic liver abscess presented during this time period in our study.

We hypothesize that increase in the incidence of amoebic liver abscess in our hospital was most likely due to the alterations in the immune state in patients of COVID 19 disease. It is important for physicians to investigate for liver abscess in patients who present again with fever and/or pain abdomen within 2 weeks of COVID 19 recovery. It will be interesting to see data from other centers in the near future.

CREDIT AUTHORSHIP CONTRIBUTION STATEMENT

Amrish Sahney - Data acquisition, analysis, manuscript writing.

Manav Wadhawan - Critical revision of the article for important intellectual content.

Nitesh Agarwal- Support in data collection and radiological image interpretation.

Neha Berry- Data acquisition.

Vishav Dadwal -Data acquisition.

Anil Vardani - Data acquisition.

Ajay Kumar- Critical revision of the article for important intellectual content and final approval of the manuscript.

CONFLICTS OF INTEREST

The authors have none to declare.

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Study has been performed by collecting data of liver abscess in covid patients.

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