

Hepatic Abscess- Management and Outcomes at Tertiary Care Center, Garhwal, Uttarakhand

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ABSTRACT

Introduction: Liver is the commonest organ prone to develop an abscess. Encountered in tropical and developing countries, this poses diagnostic/therapeutic challenges, and has significant associated morbidity. Hepatic abscess patients of varied aetiology commonly present in this setup at an advanced disease stage and warrant prompt recognition and remediation.

Aim: Study depicts and analyses management and outcome aspects of hepatic abscesses at the tertiary care center in Garhwal, Uttarakhand.

Materials and Methods: Hepatic abscess patients who presented and were managed between August 2015 and August 2019 at VCSGGMS&RI-UT were included in this observational descriptive study. Appropriate directed antimicrobial therapy was administered to all cases. Postresuscitation and evaluation based upon the indication and surgeon's preference, Percutaneous Needle Aspiration (PNA) or percutaneous USG-guided Pigtail Catheter Drainage (PCD) done, while exploratory laparotomy/Surgical Drainage (SD) done for complications.

Results: 70 patients (Total=70; 58 males=82.8%) presented with hepatic abscess, out of which 40 (57.1%) needed in-hospital treatment for severity of symptoms. PNA was done in 25 patients (35.7%), with nine (12.8%) required multiple aspirations, PCD done in seven (10.0%) and eight (11.4%) had to undergo exploratory laparotomy/SD among the 40 Inpatient Department (IPD) treated patients. Patients in this setup had a higher number of Pyogenic Liver Abscess (PLA) (48 of 70=68.6%), with E.coli predominating (26, 37.1%), than Amebic Liver Abscess (ALA) (n=17, 24.3%); most being solitary cavities (40, 57.1%), confined to the right lobe (33, 47.1%). Alcoholism (34.3%) and hypoalbuminemia (64.3%) were associated with development as well as delayed resolution of the abscess. While seven patients required repeat interventions, most gained relief from the primary treatment modality (53, 75.7%), assessed on follow-up.

Conclusion: Antibiotics and multi-modality image-guided percutaneous management resolved most hepatic abscesses. Surgeon and intervention-radiologist collaboration recommended.

Keywords: Amebic, Aspiration, Drainage, Percutaneous, Pyogenic

INTRODUCTION

Liver is the most common organ to develop abscesses, with aetiology and source varying regionally worldwide [1,2]. Prevalence of liver abscess in the Garhwal region of Uttarakhand mirrors the incidence in tropical and developing countries, including India [3-5]. PLA and ALA types constitute the majority in studies globally, while fungal, Tubercular Liver Abscess (TLA) and other rare types having a niche presence in specific patient groups [1,2,6-11]. The usual associated comorbid conditions include cirrhosis/alcoholism, diabetes, immuno-suppression from various causes, chronic renal disease, history of malignancy, age; with abscesses presenting more commonly as a solitary/unilocular cavity in the right hemiliver, in adult males. Prolonged duration fever with chills, and right upper quadrant pain with tenderness, constitutes the common presenting symptoms; other nonspecific ones may include jaundice, anorexia, nausea/vomiting, weight loss. These may accompany nonspecific alterations/derangements of hepatic enzymes on serum chemistry [1,2,12]. Ultrasonography (USG) and Contrast Enhanced Computed Tomography (CECT)/Magnetic Resonance Imaging (MRI) abdomen findings help in diagnosis as well as management of the abscess (PNA/PCD), with ruptured or complicated lesions requiring surgical management (SD) [1,2,12,13]. Examination of the aspirated contents and/or serology/blood culture determines the causative organism, against which directed antimicrobial therapy could be instituted. Systemic complications from metastatic septic lesions and rarely multi-organ failure may ensue in advanced stages [1,7,12]. Early therapeutic intervention, with infection source control, and nutritional support with lifestyle modifications later-on, mitigates the progression and

morbidity from this affliction [1,2,12-16]. Various authors, including Ghosh S, Jha AK, Sharma MP and Kumar A, Singh O et al., have also studied the management of hepatic abscess throughout India, though disease patterns of the Garhwal region, with its unique associated pathologies, are lacking [4,5,10,16]. Hence, the aim of the current study was to outline the management of patients with hepatic abscess(es) in Garhwal region.

MATERIALS AND METHODS

This observational descriptive study was undertaken at the Dept. of Surgery, at our Institute, Veer Chandra Singh Garhwali Government Medical Sciences and Research Institute, Uttarakhand (VCSGGMS&RI, Srikot, UT-246178), India, between Aug 2015-Aug 2019. Appropriate Ethical Clearance sought from Institutional Ethics Committee/IRB (IEC/VCSGGMSI&R/38/Jan 2018).

All cases of hepatic abscess, diagnosed during the above period, based upon imaging studies criteria (USG/CECT/MRI of abdomen) in those patients with relevant clinical features of pain upper abdomen accompanying fever, were included in this study, and also corroborated by serum chemistries, blood culture/serology and/or examination of aspirated cavity contents; most lesions being hypoechoic on USG or showing target-like sign on CT and those <2 cm diameter labelled as micro abscess. Notes were made of the above from the medical case record files, both during treatment and follow-up, for periods upto 6 months from presentation. All such cases of diagnosed hepatic abscess, whether new or referred, were taken into consideration during the above period, after their consent. No cases were excluded.

Those patients with severe symptoms or significant signs or constitutional symptoms, including high grade/recurrent fevers, acute pain abdomen or weakness, received in-patient treatment (40 out of 70 total), while the other stable patients were managed on an out-patient basis (30 out of 70 total), to avoid over-burdening the health-care system.

After appropriate active ongoing resuscitation with intravenous fluids and injectable supportive medications of all cases, the admitted patients were administered injectable antibiotics empirically (ceftriaxone/piperacillin, ofloxacin, amikacin, metronidazole/ornidazole, fluconazole), which were subsequently changed over to an appropriate directed therapy, once the pus and blood reports were available based upon the obtained culture and sensitivity patterns. Upon improvement of symptoms/lab parameters, they were gradually changed over to oral medications, nearing the time of discharge; whereas the outdoor-managed (OPD=Outpatient Department) patients did well on oral medications itself. The oral antimicrobial(s)/combinations were continued for durations guided by the patient's clinical/radiological recovery and dictated by the existing protocols of therapy continuation and/or change in treatment modality [1-3,13].

Postoptimisation and extensive evaluation, the IPD patients were subjected to either USG-guided aspiration PNA for small/solitary abscess (<5cm) or USG-guided PCD for large (>5cm)/multiple abscesses; SD at laparotomy was indicated for ruptured abscesses, multiple/loculated/deep-seated abscess not amenable to Percutaneous Drainage (PD) or thick viscous pus which could not be drained percutaneously, or underlying disease which requires surgical intervention (e.g., choledocholithiasis, appendicitis, etc.). The sample obtained during aspiration/drainage of abscess (IPD patients) was subjected to culture, microscopy and staining to reveal the causative organism, augmented by serology and blood culture reports (both IPD and OPD cases), enabling directed therapy to be administered against the isolated/presumed organisms and based upon the sensitivity reports according to prior established protocol [1,10-16]. Sepsis, Surgical Site Infection (SSI), malnutrition and other complications dealt with as per institutional guidelines and pre-existing protocols.

Along with their history, the clinical features pointed towards a possible diagnosis of hepatic abscess, prompting them to be subjected to further imaging of the abdomen/liver; while few patients presented as previously diagnosed cases of hepatic abscess(es) from the peripheral referral centers. USG and/or CECT abdomen were the imaging modalities utilised for confirming the diagnoses, aided by the serum chemistries.

STATISTICAL ANALYSIS

LibreOffice (libreoffice.org), LinuxMint (linuxmint.com) & Google (Office Suite/Drive) (google.com/drive) used for data analysis,

tabulation, manipulation, interpretation, graphing and charting, with results as observation numbers/percentages, statistical analyses and relevant comparisons.

RESULTS

Patients with hepatic abscess, were treated under Dept. of Surgery, VCSGMS&RI, among the background population of Garhwal region, both on out-patient (N(OPD)= 30; 42.8%) and indoor (N(IPD)= 40; 57.1%), (Total=70).

{Incidence of hepatic abscess was \approx 1/1000 surgical attendance (combined OPD visits and IPD admissions=70943, August 2015–August 2019); with higher number of PLA as compared to ALA and other aetiologic types (PLA:ALA::48:17)} [Table/Fig-1]. Most of the cases presented with complaints of right upper quadrant abdominal pain with fevers/malaise, anorexia of varying grades and durations, which on imaging pointed to the presence of hepatic abscess, and also indicated by the deranged hepatic function tests.

Male patients (82.9%; M:F::58:12) were in the age-group 20-49 years (33; 47.1%) formed the majority, with age ranges of patients from a six-year-old boy to an 81-year-old gentleman. All the patients were administered relevant antibiotics (oral in OPD treated cases; injectable/oral in IPD cases) for appropriate durations, guided by the organism sensitivity and resolution of clinical symptoms, usually for 14-21 days. All the patients were followed up with serial repeat USG/CECT abdomen, and serum chemistries done, as deemed necessary, both during treatment and follow-up.

A total 25 of the admitted patients (N(IPD)= 40) underwent PNA (nPNA= 25; 35.7%) of the abscess under USG guidance and obtained relief; nine of these requiring repeat aspiration for evacuation of the cavity contents. For those patients considered to have large abscess cavities with liquified pus contents, single/multiple pigtail catheter insertion and drainage under USG guidance was done (nPNA= 7; 10.0%), and catheter(s) removed upon resolution of the abscess, signified by reduction in daily drain output. Exploratory laparotomy followed with surgical debridement and drainage was done in eight of the patients presenting with abscess rupture and peritonitis or impending rupture or other complication(s) (nSD= 8; 11.4%) [Table/Fig-1].

Alcoholism was noted to be rampant among the catchment area population consisting of native hill dwellers among others, with hepatic abscess, and the related liver dysfunction and malnutrition was the commonest comorbidity among the patients (n Alcoholic Liver Disease (ALD)= 24; 34.3%); Diabetes Mellitus (nDM= 12; 17.1%) and immunocompromise (nImC= 9; 12.9%) of some form were other major associations found in the study. Hepato-biliary malignancy accompanying hepatic abscess was observed in three of the patients (nMalig= 3; 4.3%), during radiological study and/or histo-pathological analysis of the abscess cavity contents [Table/

Age-group years	M:F	OPD (Oral Antibiotic Therapy)	IPD					Comorbidities	Aetiologic organism	Outcomes
			USG Guided			Laparotomy & Surgical Debridement (SD)	Total IPD			
			Percutaneous Needle Aspiration (PNA)		Percutaneous Pigtail Catheter Drainage (PCD)					
			Diagnostic	Therapeutic						
≤ 19	8:1 (9)	3	2	2	1	1	6	1:0:1:0	3:2:0:1:1:3:0:1	8:1:0:0:0
20-49	27:6 (33)	14	8	4	3	4	19	5:13:3:1	15:7:2:2:2:7:1:0	26:3:2:1:1
50-74	17:4 (21)	10	4	3	2	2	11	4:7:3:1	6:5:1:1:2:5:2:1	15:2:2:1;1
≥ 75	6:1 (7)	3	1	1	1	1	4	2:4:2:1	2:2:1:0:2:2:0:0	4:1:1:0:1
Total (N)	58:12 (70) (82.9%: 17.1%)	30 (42.8%)	15	10	7	8	40 (57.1%)	12: 24: 9: 3	(Polymicrobial = 9) 26:16:4:4:7:17:3:2	53: 7: 5: 2: 3

[Table/Fig-1]: Demography/epidemiology (Aug'15-Aug'19), management and outcomes.

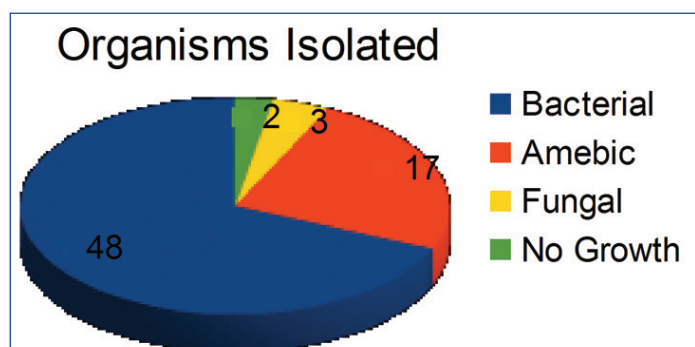
DM: A/I/C: ImC: Malig-Diabetes mellitus: Alcoholism / Cirrhosis: Immunocompromised: Malignancy; Aetiologic organisms: Ec (E.coli); KI (Klebsiella pneumoniae); Sm (Streptococcus milleri); Enterococcus faecalis; (Ef); Oth (Others)/ At (atypical); Am (Amebic-Entameba); F (Fungal-Candida); NoG (no growth); Outcomes: Recovery/Resolution, Prolonged healing, No response, Death; T/T: Treatment; IPD: Inpatient department; M: Male; F: Female

Fig-1]. Common sources of the infective foci were biliary (20; 28.6%) and portal system (17; 24.3%), besides haematogenous route (4; 5.7%) and iatrogenic (2; 2.8%).

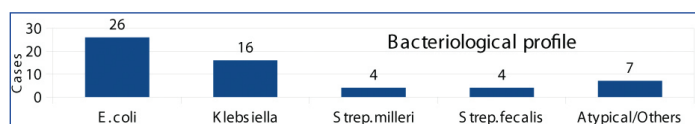
Pain right side upper abdomen and prolonged fever were the commonest presenting features for which the patients sought clinical attention. Other symptoms included jaundice, anorexia, nausea/vomiting and weight loss.

Lab abnormalities included deranged hepatic function test values, e.g., ↑ALP (n= 31), ↑AST-ALT (n= 23), ↑Bilirubin (n= 12). Hypoalbuminemia (n= 45)/anaemia (n= 35).

Examination of the aspirated/drained cavity contents or serology and blood-cultures indicated to 48 (68.6%) patients having PLA, 17 with ALA (24.3%) (anchovy sauce pus), and fungal isolates (*Candida* sp.) in three abscess cavities (4.3%), while two were negative for both culture growth or staining [Table/Fig-2a]. Among those with PLA, nine had polymicrobial isolates (12.9%). *E.coli* was the predominant bacteria identified (37.1%, n=26), whereas *Klebsiella pneumoniae* (22.9%, n=16), *Strep. Milleri* (5.7%, n=4), *Enterococcus faecalis* (5.7%, n=4), and others (including, *Staph.aureus*, *Pseudomonas*, *Proteus*, *Citrobacter*) were the other common ones in the study found in seven cases [Table/Fig-2b]. Neither anaerobes nor mycobacterium (no TLA) could be isolated in this study. Therefore, right lobe single abscess cavity PLA was the commonest finding.

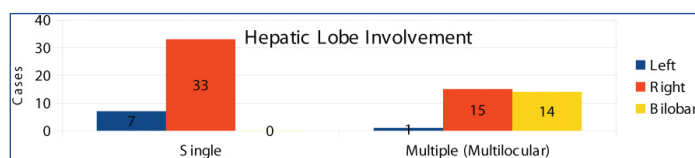


[Table/Fig-2a]: Organisms isolated.



[Table/Fig-2b]: Bacteriological profile.

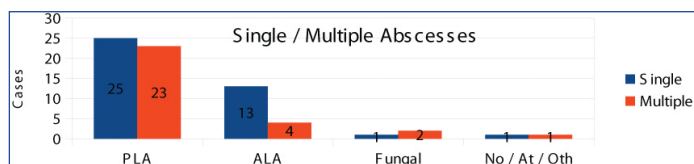
40 patients (57.1%) in the study group had a single/unilobar abscess cavity; of the remaining 30,14 (20.0%) had bilobar abscesses, while 15 (21.4%) had multilocular abscess in the right hemiliver [Table/Fig-3a].



[Table/Fig-3a]: Chart- hepatic lobe involvement.

The PLAs had an almost equal distribution among single and multiple cavities (25 single: 23 multilocular); whereas, ALA, caused by *Entameba histolytica* were mostly single cavities (13 single of 17 total) [Table/Fig-3b].

Most of the patients in the study were symptom-free by the primary intervention modality itself (53; 75.7%), whereas seven required a re-intervention (10%); delayed (5; 7.1%) or unresolved (2; 2.9%) abscesses were a concern, while three patients succumbed to the disease (4.3%). The other associated complications noted were minor SSI (18; 25.7%), pneumonia (9; 12.9%), sepsis (7; 10.0%), peritonitis (7; 10.0%) and recurrence of abscess (4; 5.7%), besides others [Table/Fig-4].

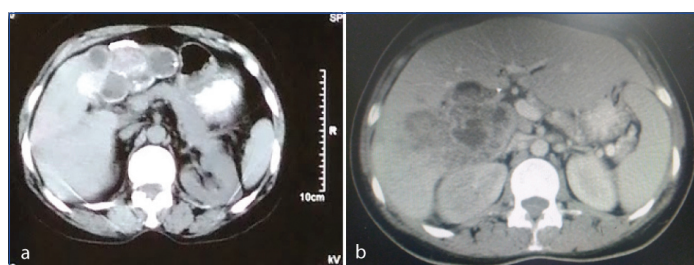


[Table/Fig-3b]: Chart-single/multiple abscesses.

Complications	Cases
Recurrent abscess	4 (5.7%)
Sepsis	7 (10.0%)
Acute renal failure	5 (7.1%)
Surgical site infection (minor/major)	18 (25.7%)
Pneumonia	9 (12.8%)
Prolonged biliary drainage	5 (7.1%)
Peritonitis	7 (10.0%)
Others	5 (7.1%)

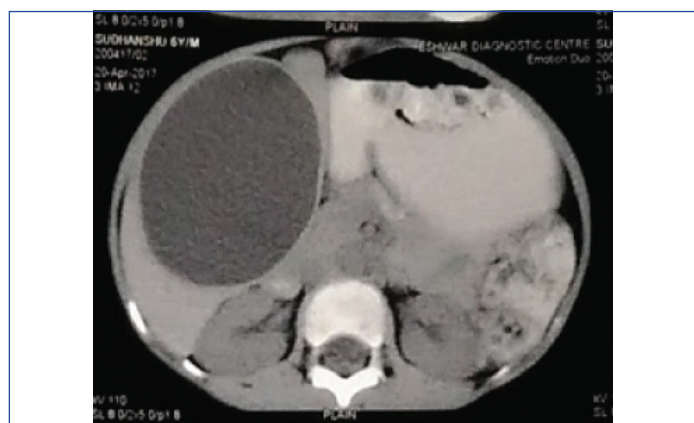
[Table/Fig-4]: Associated complications.

[Table/Fig-5a,b] depicts multilocular PLA in two middle-aged female patients: (a) bilobar; and (b) unilobar involvement; the first one underwent PCN, while the other one was managed conservatively.



[Table/Fig-5]: Pyogenic Liver Abscess (PLA); multilocular (a) bilobar/ (b) unilobar involvement in middle-aged female patients.

[Table/Fig-6] shows a large unilocular ALA, replacing most of the hepatic tissue in the right hemiliver, and the young male patient presenting with jaundice and highly compromised hepatic function with corresponding characteristic deranged LFTs; PCD was done.



[Table/Fig-6]: Amebic Liver Abscess (ALA); unilocular cavity, replacing most of the hepatic tissue in the right lobe of a young male patient, with major hepatic function test derangements.

[Table/Fig-7] shows a fungal (*Candida*) hepatic abscess in an elderly male patient, with contents of variable consistency and liquefaction in the center and areas of peripheral calcification; the patient underwent repeat PNA to gain relief.

DISCUSSION

Hepatic abscess(es) are still common in the developing regions worldwide [1-3,10]. In this study, the incidence of hepatic abscesses encountered during August 2015 to August 2019 at the tertiary care center in hill region of Uttarakhand was ≈1/1000 surgical attendance (combined OPD visits and IPD admissions = 70943); with higher



[Table/Fig-7]: Fungal hepatic abscess, with atypical features; multiloculated, in the right hemiliver of an elderly male patient.

number of PLA as compared to ALA and other aetiologic types (PLA:ALA::48:17). These findings were consistent with those of Sharma MP and Kumar A and Mavilia MG et al., [10,11], while other studies by Ghosh S et al., Jha AK et al., Singh O et al., showed a higher incidence of ALA compared to PLA in their study groups [4,5,16]. The observation of higher incidence of middle-age/elderly male patients (62.8%) with dominance of unilocular right hemiliver abscess (47.1%) for both PLA and ALA, is comparable with the above studies [4,5,8,9,11,12,14-16] and others around the world [1-3]. Malnutrition (hypoalbuminemia, anaemia) or some form of immune-suppressed state, including DM, alcoholism, contributed to the development of hepatic abscess [1-4,11,12]. Most of these studies [1-5,10-16] also point to the predominance of Gram negative aerobes (*E.coli*, *Klebsiella*), followed by Gram positive aerobes, or polymicrobial infections in cases of PLA, usually of biliary origin (gallstone related) or a portal source (due to appendicitis, diverticular disease, etc.), similar to present study findings. TLA (caused by *Mycobacterium tuberculosis*) and other atypical types of hepatic abscess are uncommon; and usually present as solitary (TLA)/multiple (atypical) small abscesses in the liver; there were no such cases in this study [1,4,10].

Ghosh S et al., and Jha AK et al., have shown in their respective studies that hepatic abscess is more common in alcoholics, diabetics and/or of lower socioeconomic class; they mostly present as a solitary cavity with right lower lobe involvement, and have a higher number of younger individuals affected [4,5]. Most of these findings were consistent with present study except for the higher involvement of middle-aged/elderly individuals and more of PLA cases as compared to ALA. Mavilia MG et al., had also implicated diabetes and other immunocompromised states/malignancies in the causation of hepatic abscesses, but found PLA to be more common among the studied populations [11]. Fiore M et al., and Lipsett PA et al., have found that frequency of hepatic abscess caused by fungi (*Candida* sp.) is rising among immunocompromised patients and those with haematologic and other malignancies [8,9]. Sharma MP and Kumar A has discussed about some unique aspects of paediatric hepatic abscesses, including associations with genetic factors, parasitic and other abdominal infections, trauma abdomen, etc., playing a greater role in the causation, with higher numbers of PLA and sometimes involvement of unusual or fungal/tubercular organisms [10]. Alvarez JAP et al., has shown that multiple liver abscesses comprise a disease of biliary origin, and are associated with higher age, longer symptomatic periods, and also higher mortality rate than in single abscess, and further state that antibiotics have a greater role to play in such cases of multiple abscesses [12].

Abdominal imaging in patients with prolonged right upper abdominal pain and fever helps to clinch the diagnosis, aided by the variably deranged LFT and blood component test values, as noted above. Most hepatic abscesses can be treated in collaboration with the

interventional radiologist, while complicated and severe presentations necessitate timely surgical intervention, and occasionally critical care support; those presenting early in the disease course or with minor involvement may be managed on an OPD basis. Prolonged treatment with directed specific antimicrobial therapy against the etiologic organism is pertinent, based upon the aspirate examination and serology / blood-culture findings, accompanied with simultaneous management of the infection source focus and any primary pathology. Nutritional buildup, de-addiction and lifestyle modifications during follow-up are important adjuncts to wholesome therapy, speeding up recovery and reducing morbidity/mortality.

Heneghan HM et al., found PLA to be uncommon with decreasing mortality trends now-a-days with improved treatment modalities, including radiological interventions and antimicrobial therapy forming the mainstay; and surgical intervention considered for patients with large, complex, septated or multiple abscesses, underlying disease or in whom PD has failed [14]. Singh O et al., had iterated that PCD is a better treatment option than PNA for the management of large liver abscesses (of size >10 cm), in terms of duration to attain clinical relief and duration for which parenteral antibiotics are needed [16]; while, Tan YM et al., has stated that SD provides better clinical outcomes than PD, and to be considered as first-line treatment of large liver abscesses as it produces equally good mortality outcomes as PD [15]. The present study found that radiological intervention procedures were better suited and tolerated by most patients, while those with obvious features of rupture/acute abdomen or other ominous symptoms benefitted from open surgical procedures.

Entamoeba histolytica, spread by feco-oral route, is endemic in India and usually manifests as amebic dysentery or ALA. Rupture of ALA can occur into the pleural/peritoneal cavity or rarely an adjoining organ [1,3,6]. It may be treated empirically with metronidazole, followed by a luminal amebicide, with large/complicated ALA requiring intervention, while radiologic resolution may take several months [4-6]. Fungal (*Candida* sp., others) hepatic abscess results from invasion from the gastrointestinal tract into the bloodstream, usually in immunosuppressed or those with haematological malignancies. Prolonged duration antifungal therapy and PNA when indicated, are the available treatment choices [7-9].

Clinical Implications: Preventive measures, including treating diabetes and alcoholism, seeking early treatment of infection source focus and better hygiene practices among populations takes precedence. Policy of speedy referral of suspected/confirmed cases of hepatic abscess to a surgeon cannot be understated. Image-guided treatment modalities, in consultation with interventional radiologist, constitute the treatment of choice for hepatic abscesses. Nutritional buildup, de-addiction and lifestyle modifications during follow-up are important adjuncts to wholesome therapy, speeding up recovery and reducing morbidity/mortality.

Limitation(s)

Some of the limitations plaguing this study, included a small sample size resulting from a smaller catchment area population, some of the referred cases from Departments of Medicine & Paediatrics respectively, either not reporting to the Department of Surgery or being lost to follow-up, technical restraints, in terms of nonavailability of CT-guided intervention, no polymicrobial/anaerobic organism isolation by the Microbiology lab, etc., and of course, the "admission bias" among patients from various sections of the society.

CONCLUSION(S)

Most hepatic abscesses presenting early in the disease course or with minor involvement may be managed on an OPD basis, severe presentations necessitate timely surgical intervention, and occasionally critical care support. Prolonged treatment with directed specific antimicrobial therapy against the aetiologic organism is pertinent, based upon the aspirate examination and serology/blood-

culture findings, accompanied with simultaneous management of the infective source focus and any primary pathology.

Author contributions: KA main author, for conceptualising and carrying out the study, article composition; BS for providing guidance/inputs in the study and academic assistance; VDA is the interventional radiologist assisting in the case management; SK for pathology/microbiology assessments of samples.

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