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PEER-REVIEW REPORT

Name of journal: *World Journal of Radiology*

Manuscript NO: 76077

Title: Amebic liver abscess: Clinico-radiological findings and interventional management

Provenance and peer review: Invited manuscript; externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 06264489
Position: Peer Reviewer
Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: United States

Author's Country/Territory: India

Manuscript submission date: 2022-02-28

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Reviewer accepted review: 2022-03-05 17:32

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Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [Y] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [ ] Grade B: Minor language polishing [Y] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [Y] Major revision [ ] Rejection
Re-review	[ ] Yes [Y] No

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Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

I really like the idea of correlating imaging findings, lab findings, and clinical status to types of ALA. This could be helpful for prognostication and the decision for intervention. This could be a helpful way to stratify these variable patients. However, I do not feel that the paper provides convincing evidence for radiologic stratification as stated currently. There are few references or statistics connecting clinical course to imaging findings in the paper. Additionally, given the review's emphasis on clinicoradiological findings, there is too much emphasis on pathogenesis. It could be helpful to create a figure breaking down the radiologic, clinical, and management considerations unique to the three types of ALA. If the paper was streamlined with concise breakdowns of clinical presentations and radiologic findings for each patient type followed by management considerations for each patient type, it would be a very helpful manuscript. Additionally, there are many grammatical and syntax errors that if corrected would greatly improve the manuscript. I have included some other recommendations and thoughts by page below. General: - Many of the references included earlier on are other reviews. Would try and include primary sources of information, especially when a review is used for a single point made in the manuscript Page 2 Line 9 - delete “the” before antibiotics Line 10 - do not need “frequently” twice Line 20-22 - each line repeats the same concept, could be more concise Page 3 Line 13 - It mentions there are only two forms here, but a third form is mentioned earlier: mild form Page 4 Line 3 - please clarify that EH is not a natural colonizer, but only colonizes those who have been exposed and even they are not all colonized for life Line 5 - Can be restated just that ALA is the most common and has the highest mortality of amebiasis manifestations Line 7 - “Estimates” instead of

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"estimated" Line 5 - references are quite old and may have some less than modern epidemiological estimations Line 12 - please include citation for mortality reduction Line 13 - Given the statement that most patients are asymptomatic at baseline, please give context for "becoming asymptomatic" Line 14 - can delete "It is considered that" Page 6 Line 5 - "Even in endemic countries, ALA occurs primarily in rural areas where defecation in open air is a common practice" would include citation for this Line 13-15 Multiple lines that repeat same idea, could be more concise Page 7 Line 10 - 1% is quoted as frequency of ALA, but 1-10% is used earlier in the manuscript Page 8 Line 11 - Would clarify this is a mature wall that indicated chronicity/2' infection as opposed to the wall mentioned as ragged in line 3 Line 15 - Wording is somewhat misleading as it says above they are usually solitary, but that 60% of autopsy samples have multiple. Is this because autopsy samples are from patients with more severe courses? Or is it because imaging findings are incongruent with post-mortem findings? Line 17 - Please define "western" populations vs asian populations Page 9 Line 7 - Finding instead of findings, but this line can also be removed as it mentioned immediately above Line 9 - Most patients with have elevated Alkaline Phosphatase and some but not all patients will have transaminitis. There is even some suggestion they can be used to predict size of abscess/severity of disease (http://dx.doi.org/10.18203/2320-6012.ijrms20173158) Line 17 - "The prevalence of this type of ALA may be high in endemic areas (up to 60%)." —> would include citation Line 20 - Number 18 is present without context Page 11 Line 16 - Would address the lack of specificity and frequency of seropositivity in endemic countries considering this is the population of interest for the severe subtypes and how this can make diagnosis difficult Page 12 Line 12 - "Most common employed modalities" —> for diagnosis of ALA Line 15 - Would add citation for why MRI seems to offer no advantage Page 13 Line 2 - Would include numbers in terms of sensitivity/specificity between CT/US for diagnosis to improve this claim Page 18

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"The diagnosis of superinfection can be made when the needle aspirate changes its odor and color from odorless and chocolate-brown color to foul smelling and purulent [14, 43]." - I do not think this is supported by the works cited, and does not seem reliable method of this determination "On imaging, the secondarily infected abscesses demonstrate rim enhancing wall (type II pattern) similar to pyogenic abscesses." - needs citation Page 20 Most experts recommend therapy with an intraluminal agent after metronidazole for elimination of potential intraluminal cysts Section: Imaging classification and clinicoradiological correlation - I feel that this section is the crux of the paper and has little to no clinical data to support the type of imaging seen and its connection to the patient outcome. How is the connection between the imaging and clinical course made? Is it based on case series, personal experience? Please elaborate.

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Provenance and peer review: Invited manuscript; externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 00058381
Position: Editorial Board
Academic degree: MD

Professional title: Professor

Reviewer's Country/Territory: Austria

Author's Country/Territory: India

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Reviewer accepted review: 2022-04-14 07:46

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Review time: 1 Day and 5 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [Y] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [ ] Grade B: Minor language polishing [Y] Grade C: A great deal of language polishing [ ] Grade D: Rejection
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Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Main Comments: (1) This manuscript deals with amebic liver abscess, its diagnosis, classification and treatment. The authors provide an overview on the subject, focusing on severe and complicated subtypes; illustrative pictures are included. (2) Many repetitions within the text make it lengthy for the reader, please be more concise. (3) As for the clinico-radiological correlation, more robust data/citations would be expected. Specific Comments/Suggestions: (4) Risk factors, page 6: "Additionally, the disease in men is more complicated than women" -> Additionally, the disease is more complicated in men than in women. (5) Pathogenesis (second paragraph), page 8: "liquefied necrotic tissue (chocolate-colored sterile pus)" -> liquefied necrotic tissue (chocolate-colored sterile "pus"). (6) Clinical presentation, page 9: "The typical findings on physical examination is hepatomegaly with point tenderness in the intercostal spaces" -> The typical finding on physical examination is hepatomegaly with point tenderness in the intercostal spaces; "and an exquisitely tender hepatomegaly 18" -> and an exquisitely tender hepatomegaly [18]; "…present In fact…" -> …present. In fact… (7) Clinical presentation, page 11: "Leukocytosis in chronic abscesses suggest the presence of secondary infection" -> Leukocytosis in chronic abscesses suggests the presence of secondary infection. (8) Imaging evaluation, page 13: "The overall diagnostic accuracy of CT is more than ultrasound" -> The overall diagnostic accuracy of CT is higher than of ultrasound. (9) Imaging classification and clinicoradiological correlation, page 14: "the viable parenchyma that are yet to be necrotic" -> the viable parenchyma that is yet to be necrotic. (10) Rupture, page 15: "However, intrathoracic ruptures, particularly the intrapulmonary, is noted more frequently in chronic cases (type II or III abscesses)" ->

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However, intrathoracic ruptures, particularly the intrapulmonary ones, are noted more frequently in chronic cases (type II or III abscesses). (11) Intrathoracic rupture: Pleural empyema, Lung abscess, Hepatobronchial fistula, page 16: "invading through the both diaphragm and pleura" -> invading through both diaphragm and pleura. (12) Biliary complication: communication versus compression, page 18: "total bilirubin levels >2 mg/dL was present only in the patients with biliary complications" -> total bilirubin levels >2 mg/dL were present only in the patients with biliary complications. (13) Concurrent Colitis and Perforations, page 19: "diarrhea is found only in only 15 to 30% of patients with ALA" -> diarrhea is found in only 15 to 30% of patients with ALA. (14) Management: Role of image-guided percutaneous drainage (third paragraph), page 21: "In addition to clinical criteria, imaging based criteria for the use of drainage was formulated by De la Rey Nel et al., which is still widely used [8-10, 52]. They recommended that the abscesses greater than 10 cm should be drained as it takes a long time to resolve and are at risk of all types of complications. Furthermore, they suggested that the abscesses located in the left should be drained as it carries risk of rupture into the pericardium, a fatal complication with a high mortality" -> In addition to clinical criteria, imaging based criteria for the use of drainage, which are still widely used, were formulated by De la Rey Nel et al. [8-10, 52]. They recommended that the abscesses greater than 10 cm should be drained as they take a long time to resolve and are at risk of all types of complications. Furthermore, they suggested that the abscesses located in the left lobe should be drained as they carry a risk of rupture into the pericardium, a fatal complication with a high mortality. (15) Needle aspiration versus catheter drainage, page 23: "abscesses that liquefies over a period of time" -> abscesses that liquefy over a period of time. (16) Percutaneous drainage in management of complications (third paragraph), page 23: "it also effectively treats pleuropulmonary ruptures 14" -> it also effectively treats pleuropulmonary ruptures [14]. (17) Figure legend 4: "for more than

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4-weeks" -> for more than 4 weeks. (18) Figure legend 5: "The fluid collection that is localized in the subphrenic space (asterisk)" -> A fluid collection is localized in the subphrenic space (asterisk). These are just examples; a substantial overall improvement of the manuscript would be suggested in order to make it fit for publication.

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Provenance and peer review: Invited manuscript; externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 02845080
Position: Peer Reviewer
Academic degree: DNB, FICS, FRCS (Gen Surg), MBBS, MMed, MNAMS, MS

Professional title: Associate Professor, Director, Surgical Oncologist

Reviewer's Country/Territory: Singapore

Author's Country/Territory: India

Manuscript submission date: 2022-02-28

Reviewer chosen by: Qi-Gu Yao

Reviewer accepted review: 2022-04-16 12:49

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Scientific quality	[Y] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[Y] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
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Peer-reviewer statements	Peer-Review: [ ] Anonymous [Y] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

I enjoyed reading the manuscript. I understand the focus is narrow - uncomplicated abscess is not discussed. 1. You have described 3 types of ALA - including subacute mild and thus i feel omit the "complicated" from the title. I feel this review should apply to every ALA - regardless of uncomplicated or complicated. Agree that you did focus on complicated more. 2. I find some fault with 3 citations for one study - pls check this. In a study of 317 patients with ALA, Balasegaram reported acute fulminating infection in 13% of cases [13, 20,51]. 3. Citation 18 is improper format - check it. The patients often present more acutely (< 10 days) with signs of severe disease including systemic toxicity, high fevers and chills, and an exquisitely tender hepatomegaly 18. 4. Full stop is missing from the sentence - Signs related to rupture and other complications may be present 5. Nice images. I feel sometimes the type II and type III can be confusing on the CT scan if the contrast enhancement is faint or if the IV contrast is suboptimal and sometimes if patient is already on therapy than though by timepoint patient may qualify as subacute; he may have features of chronic ALA. Some discussion on this is necessary. Is this classification validated? Need some comments and discussion. 6. Full form of ERCP is needed. Check this - In such cases, the diagnosis may be confirmed when ERCP or cavitogram demonstrates contrast extravasation into the abscess cavity [54]. 7. Also need to add that stenting or sphincterotomy are essential to control bile leak prior to abscess drain removal. 8. The following statement is correct and i hope you could add some discussion that the contrary is true for pyogenic abscess. Check this -""The pus cultures rarely yield positive results. This is because most patients are generally pretreated with antibiotics."" In general, blood culture is negative for pyogenic liver

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abscess but pus culture is positive. This is contrary to what you mention for ALA (i do agree with you). Needs 1-2 sentences to compare and contrast. 9. I dont see any mention on laparotomy or laparoscopy and any data being included in the discussion section. Pls check and if literature mentions, include 2-3 sentences in this. 10. I also dont see mention about CRP or Procalcitonin role in diagnosis. I see white cell count stated. May be add 1-2 sentences on CRP or procalcitonin (if any data have).

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RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: *World Journal of Radiology*

Manuscript NO: 76077

Title: Amebic liver abscess: Clinico-radiological findings and interventional management

Provenance and peer review: Invited manuscript; externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 00058381
Position: Editorial Board
Academic degree: MD

Professional title: Professor

Reviewer's Country/Territory: Austria

Author's Country/Territory: India

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Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Peer-reviewer	Peer-Review: [Y] Anonymous [ ] Onymous

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statements	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The authors have revised their manuscript according to the recommendations. Comments/Suggestions: (1) Laboratory evaluation, first paragraph: "Moreover, the serological tests may be negative in the first seven to ten days of the infection, limiting its diagnostic use for acute ALA[7]." -> Moreover, the serological tests may be negative in the first seven to ten days of the infection, limiting their diagnostic use for acute ALA[7]. (2) Imaging evaluation, third paragraph (first sentence): "On MRI, variable degree of wall formation and edema surrounding ALA have been reported according to the status of abscess healing." -> On MRI, variable degrees of wall formation and edema surrounding ALA have been reported according to the status of abscess healing. (3) Imaging evaluation, third paragraph (penultimate sentence): "It appears that imaging findings of ALA can be classified into three distinct but overlapping patterns (type I, II and III) that correlates well with the clinical subtypes (Table 1)[10]." -> It appears that imaging findings of ALA can be classified into three distinct but overlapping patterns (type I, II and III) that correlate well with the clinical subtypes (Table 1)[10]. (4) Type III abscess: ALA with non enhancing wall[10]: "Clinicians should be aware that healed ALAs in this pattern often resemble cyst and can persist for months or years following successful treatment[46,66,71,72]." -> Clinicians should be aware that healed ALAs in this pattern often resemble cysts and can persist for months or years following successful treatment[46,66,71,72]. (5) Intraperitoneal Rupture: Contained Rupture Versus Free Rupture: "The free rupture is characterized by the fluid collection that diffusely involves the entire peritoneal cavity; they can cause generalized peritonitis and carry a poor prognosis (Figure 6)." -> The free rupture is characterized by the fluid collection that diffusely involves the entire peritoneal cavity; it can cause generalized peritonitis and

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carry a poor prognosis (Figure 6). (6) Biliary Complication: Communication Versus Compression: "The large (> 5 to 10 cm) and centrally located abscesses (near porta hepatis) are more likely to have biliary compilations than those smaller and have subcapsular locations[12]." -> The large (> 5 to 10 cm) and centrally located abscesses (near porta hepatis) are more likely to have biliary compilations than those smaller and with subcapsular locations[12]. (7) Key words: "Ruptured amebic liver abscess" -> ruptured amebic liver abscess.