



## Amoebic liver abscess — results of a conservative management policy

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**Objective.** To evaluate the safety and efficacy of conservative management of amoebic liver abscesses.

**Design.** A prospective study carried out over a 1-year period.

**Setting.** Inpatients and outpatients in a tertiary referral institution.

**Subjects.** Amoebic liver abscess was diagnosed on clinical, ultrasonographic, and serological features. All patients were treated with metronidazole. The indication for ultrasound-guided aspiration of the abscess was failure to improve clinically within 48 - 72 hours.

**Main outcome measures.** Clinical improvement, clinical deterioration and failure of clinical improvement (persistent pain).

**Results.** In total 178 patients (male-to-female ratio 5:1) with 203 abscesses were treated during this period. Of these, 23

patients required percutaneous aspiration and 150 patients were managed without intervention and clinically resolved spontaneously. Abscesses requiring aspiration tended to be larger than those managed without aspiration (10.7 cm v. 8.2 cm) ( $p = 0.003$ ). There were no complications following aspiration. Mean hospital stay was longer (12.3 days) for patients who underwent aspiration compared with those who did not (6.7 days) ( $p = 0.031$ ). Only 5 patients presented with ruptured abscesses, 1 cutaneously and 4 intraperitoneally, with the only death in this latter category.

**Conclusion.** Conservative medical management of amoebic liver abscess is safe. Percutaneous ultrasound-guided aspiration is indicated only in patients who fail to improve clinically after 48 - 72 hours rather than on rigid criteria.

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Dysenteric illness is the most common form of symptomatic *Entamoeba histolytica* infection, which is essentially a disease of developing countries.<sup>1,5</sup> Amoebic liver abscess (ALA), a very common extra-intestinal manifestation of amoebiasis, arises as a result of spread of *E. histolytica* from the large bowel to the liver via the portal vein.<sup>2,4,6</sup> The amoebae then induce multiple small infarcts, which coalesce to form larger abscesses, which are separated from the normal liver by a hyperaemic oedematous zone.<sup>3</sup>

Management of uncomplicated ALA involves medical treatment with oral or intravenous metronidazole with or without percutaneous aspiration. This treatment leads to fibrous capsule formation around the abscess, thereby preventing abscess extension and subsequent rupture.<sup>3,7</sup> If untreated the abscess enlarges, with a risk of rupture into contiguous structures,<sup>1,3,5,8</sup> which is the main reason

management algorithms have been developed to aspirate those abscesses perceived to be at increased risk of rupture. The disadvantages of percutaneous aspiration are its invasiveness and predisposition to secondary infection.

We contend that most abscesses will resolve on medical treatment without the need to resort to aspiration and that aspiration should be restricted to patients who fail to improve on medical management for 48 - 72 hours. We undertook this prospective study to evaluate the safety and efficacy of this approach.

### Patients and methods

The study analysed all ALAs presenting to King Edward VIII Hospital in Durban from 1 July 1997 to 30 June 1998. Patients with the classic triad of right upper quadrant pain, hepatomegaly and low-grade fever were suspected of having ALA and were subjected to ultrasonography and an amoebic gel diffusion test (AGDT). The ultrasonographic features were hypoechogenic, round or oval lesions without septa (Fig. 1). An AGDT reactive at 20 hours was regarded as positive. All patients were given metronidazole 800 mg orally or 500 mg intravenously three times a day for two weeks.

Indications for ultrasound-guided percutaneous aspiration were clinical deterioration, failure of clinical improvement (persistent pain) within 48 - 72 hours or suspicion of a

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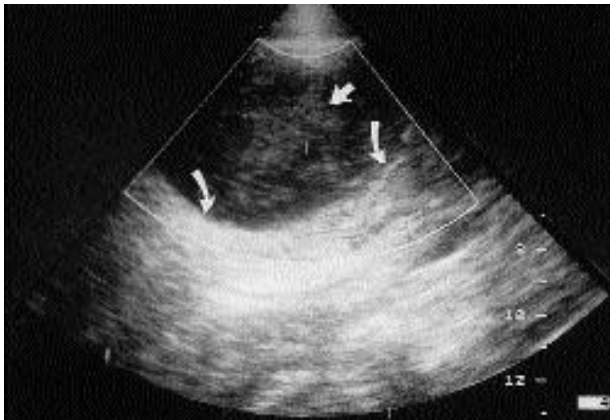


Fig. 1. Photograph of an ultrasound scan showing a cavity with echoes within it (straight arrow). The edge of the abscess is indicated by curved arrows.

secondarily infected abscess. The latter condition would be suspected if patients were toxic with high fever and leucocytosis. Clinical improvement was defined as reduced abdominal tenderness, decreased tachycardia, tachypnoea and temperature. Aspiration was performed under local anaesthetic with a 14 - 16-gauge needle placed under sterile conditions with ultrasound guidance. Abscesses were aspirated to dryness or, if this could not be achieved, a Stamey catheter was left *in situ* to drain in the ward until drainage was < 20 ml/24 hours. Patients were followed up for 1 - 4 months following discharge from hospital, but not to ultrasonographic resolution. The Student's *t*-test was employed to determine the extent of evidence for statistically distinguishable differences in abscess diameter and hospital stay and the Mann-Whitney U-test was employed to distinguish between hospital stay for large (> 8 cm) and small (< 8 cm) abscesses.

**Results**

Of a total of 189 patients treated for ALA only 178 had a positive AGDT and were analysed. The other 11, with a negative AGDT despite clinical and ultrasonographic features of ALA, were treated as ALA but excluded from the study. The patient profile is shown in Table I. Fig. 2 illustrates the monthly distribution of patients with ALA over the year. The peak was in June and July.

Table II shows management of all 178 patients. Seventy-six patients had mild symptoms and were managed successfully as outpatients. The other 102 patients were treated as inpatients, of whom 74 improved on medical treatment within 48 hours. The two patients with associated amoebic colitis improved clinically on inpatient treatment.

Some 23 patients (13%) required ultrasound-guided aspiration because of failure to improve within 48 - 72 hours, 8 from the left lobe (14%) and 15 from the right lobe (10%) (*p* =

**Table I. Patient profile**

Total admissions (excluding trauma and obstetric cases) (N)	33 173
Total number of patients with ALA	189
Hospital prevalence of ALA(%)	0.5
Exclusions (N)	11
Total number of patients analysed (with ALA)	178
Male-to-female ratio	5 : 1
Mean age (years)	39.11 ± 13.31
Patients with right lobe abscesses (N)	120
Patients with left lobe abscesses (N)	33
Patients with bilateral abscesses (N)	25
Patients with uncomplicated ALA (N)	173
Patients presenting with ruptured ALA (N (%))	5 (2.8%)
Intraperitoneal rupture (N)	4
Cutaneous rupture (N)	1
Patients with associated amoebic colitis (N (%))	2 (1%)

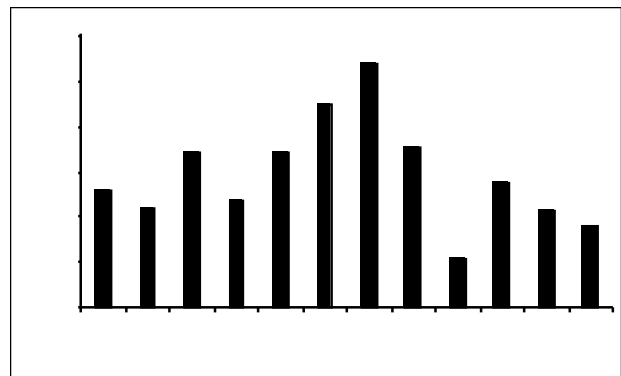


Fig. 2. Monthly distribution of amoebic liver abscess in 178 patients.

**Table II. Management of 178 patients with amoebic liver abscesses (N)**

	Percutaneous			Total
	Clinical	drainage	Laparotomy	
Outpatient	76	0	0	76
Inpatient	75	23	4	102
<b>Total</b>	<b>151</b>	<b>23</b>	<b>4</b>	<b>178</b>

0.913). Two of these patients with large right lobe abscesses underwent continuous drainage of the abscesses using the Stamey catheter. Two patients had a negative initial AGDT and were subjected to aspiration as they failed to improve on metronidazole and pyogenic abscesses could not be ruled out. Subsequent AGDT was positive in both patients. Five patients out of the whole group had abscesses abutting on the diaphragm, 1 of whom required aspiration according to our criteria. Fig. 3 stratifies left and right lobe abscesses according to size and need for aspiration.

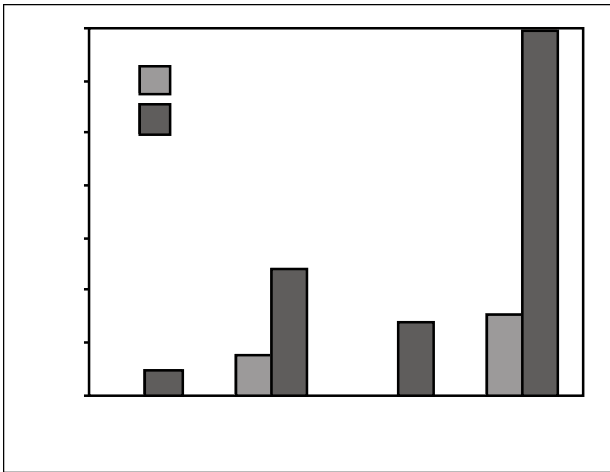


Fig. 3. Stratification of amoebic liver abscesses according to size, site and aspiration.

Five patients presented with ruptured ALA(3%). Four of these patients with peritonitis were subjected to laparotomy where the diagnosis of an intraperitoneal rupture was made and subsequently confirmed by a positive AGDT. All required admission to the intensive care unit, but one of them died of multiple organ dysfunction. Another patient, who was admitted with rupture of the abscess to the skin, was treated conservatively with resultant good resolution.

The diameter of the abscess indirectly reflects on abscess size. The mean diameter of aspirated abscesses was  $10.7 \pm 3.9$  cm (range 7.4 - 19 cm) compared with  $8.2 \pm 3.8$  cm (range 2.3 - 20 cm) for non-aspirated abscesses, a statistically significant difference ( $p = 0.003$ , 95% confidence interval (CI) 1.3, 5.3). There were no complications in aspirated patients.

Mean hospital stay for the whole group was  $10.43 \pm 8.61$  days (range 2 - 41 days),  $13.4 \pm 9.7$  days for aspirated patients compared with  $8.4 \pm 7.4$  days for non-aspirated patients ( $p = 0.031$ , 95% CI 0.45, 8.88). Table III shows the influence of size on hospital stay relative to aspiration. Although aspirated patients, both with small and large abscesses, had a longer hospital stay this did not reach statistical significance. The hospital stay for the 3 patients who survived following laparotomy was 11 - 25 days. The patient who died had been in the intensive care unit for 36 days. The patient with rupture of ALA to the skin was hospitalised for 13 days.

Table III. Influence of size and aspiration on hospital stay

Size (cm)	Aspirated (days)	Not aspirated (days)	p-value
< 8	11.3 + 10.1	9.1 + 9.1	0.09
8	11.9 + 9.2	9.2 + 6.5	0.31
p-value	0.71	0.31	

## Discussion

Although ALA is traditionally a summertime disease, there was a winter month peak in this series. This anomaly can be explained by the long incubation period of *E. histolytica* that has been demonstrated in travellers from Europe who develop ALA about 8 - 20 weeks after leaving an endemic area.<sup>1</sup> There was a hospital prevalence of 0.5% in this series. Two other studies from this institution have reported on amoebic liver abscess. Adams and MacLeod<sup>2</sup> reported an admission rate of 103 patients per year over a 20-year period. De la Rey Nel *et al.*<sup>7</sup> reported 411 admissions in 1 year. Neither reported their hospital prevalence. Our current annual load a decade later is half that reported by De la Rey Nel *et al.*<sup>7</sup> There were only 2 patients with proven amoebic colitis in the present series. Sachdev and Dhoi<sup>8</sup> performed colonoscopy or sigmoidoscopy in 45 patients with ALA and demonstrated that there was colonic involvement in 58% of cases although only 3 of 45 had diarrhoea.

The efficacy of metronidazole as an amoebicide is well documented with a 90% cure rate and no resistance having been observed.<sup>1,3</sup> Our 2-week treatment regimen with metronidazole has been shown to be effective,<sup>3,7</sup> although a single daily dose of 2.4 g orally is also effective.<sup>1,3,8</sup> The role of percutaneous aspiration in ALA is debated. Adams and MacLeod<sup>2</sup> used both metronidazole and aspiration, with good results. In his series of 192 ALAs, Luvuno<sup>3</sup> in 1988 showed that the majority of ALAs healed without aspiration. In 1989 De la Rey Nel *et al.*<sup>7</sup> tried to establish which patients were unlikely to heal without aspiration. They suggested failure to improve within 48 - 72 hours, abscesses causing marked tenderness or severe pain, large abscesses (> 10 cm), superficial abscesses, marked elevation of the diaphragm, left lobe abscesses adjacent to the diaphragm and negative AGDT as possible sufficient indications for aspiration. Akgun *et al.*<sup>4</sup> and Tandon *et al.*<sup>9</sup> advocated aspiration in abscesses that were > 5 cm in diameter. Saraswat *et al.*<sup>10</sup> used non-response to medical therapy, imminent rupture, ruptured ALA, enlarging abscess, persistent symptoms or large left lobe abscesses as indications for aspiration. The argument for aspiration by these authors was to reduce the rupture rate to which these circumstances would predispose the abscess. We believe that these indications for aspiration are too liberal and currently the only indication for aspiration in our practice is lack of clinical improvement, which is based on the recommendations of local studies.<sup>3</sup> De la Rey Nel *et al.*<sup>7</sup> and Adams and MacLeod<sup>2</sup> did not specify the sizes of the abscesses in their respective series, although De la Rey Nel *et al.*<sup>7</sup> suggested size as one of the criteria for aspiration.

There were 23 abscesses (13%) managed by percutaneous aspiration in this series. This is much lower than aspiration rates of 46 - 59% reported in the literature.<sup>7,10</sup> If we had adopted the criteria of Tandon *et al.*<sup>9</sup> and De la Rey Nel *et al.*<sup>7</sup> we would



have aspirated 36% and 23% of abscesses respectively; we therefore avoided aspiration in 23% and 10% of patients respectively. Of the 5 patients with abscesses abutting on the diaphragm only 1 (20%) required aspiration in this series, thereby eliminating aspiration in 80% of 5 cases. This reduction and subsequent favourable outcome supports the view that proximity to the liver surface is not an absolute indication for aspiration. We do not subscribe to the view that left hepatic lobe abscesses must be treated more aggressively by aspiration on the basis that they are more likely to rupture into the pericardium as suggested by some authors.<sup>1</sup> Secondary infection, which occurs in 2% of cases following percutaneous aspiration,<sup>11</sup> did not occur in this series.

While some authors believe that only abscesses of less than 5 cm will respond to medical treatment<sup>4</sup> and that bigger abscesses should undergo aspiration, we have shown that abscesses of all sizes respond well to medical treatment, although abscesses requiring aspiration tended to be large. Patients with aspirated abscesses tended to stay longer in hospital irrespective of abscess size, suggesting that aspiration and not abscess size was the factor most influencing hospital stay.

Akgun *et al.*<sup>4</sup> reviewed their experience in 44 patients with ALA. Their medical treatment consisted of a 10-day course of metronidazole 2 250 mg per day in divided doses and tetracycline 750 mg in divided doses per day. Seventy-three per cent did not respond to medical treatment and were offered aspiration only after 7 days of treatment. Of these patients 28 (88%) responded to aspiration and the remaining 4 required surgery. These authors did not list their indications for surgery in the manuscript. The 73% is a high failure rate for metronidazole treatment and is not in keeping with our findings and those of other authors.<sup>1,3,7,8</sup> In this series, which is over twice as large as that of Akgun *et al.*,<sup>4</sup> we had a much smaller percentage that failed medical therapy alone or with aspiration and we have resorted to catheter drainage only twice. Drainage is as effective as and much less invasive than open operation.

There is no agreement regarding the optimal length of waiting time required before failure of medical treatment can be declared and percutaneous aspiration resorted to. Mondragon-Sanchez *et al.*<sup>12</sup> advise treatment with metronidazole for 48 hours and advocate percutaneous aspiration if there is no response. We are in agreement with the 48-hour approach and we have used 48 - 72 hours as a cutoff point in the present study. We do not agree with the approach of Akgun *et al.*<sup>4</sup> who wait 7 days before offering percutaneous aspiration.

Many investigators<sup>9,10</sup> have demonstrated that aspiration is safe and effective and that it leads to early resolution and shorter hospital stay. Although we echo their enthusiasm with regard to safety and efficacy of percutaneous aspiration we

were not able to demonstrate shorter hospital stay following aspiration.

The most serious complication of an amoebic liver abscess is rupture into adjacent vital structures such as the chest (4 - 20%),<sup>1,2,8</sup> peritoneum (2 - 10%)<sup>1,2,8</sup> and pericardium (0.8 - 3%).<sup>2,7,8</sup> The present study has shown a very low spontaneous rupture rate of 3% (5 out of 178). We note with interest that the earlier annual rupture rate in the same institution remained 10% over two decades,<sup>2,7</sup> but has dropped to 3% a decade later. We can only postulate that the reason for the low rupture rate in this series is early presentation of the patients to hospital, and more liberal use of metronidazole in the community for the treatment of dysentery.

Conservative management of intraperitoneal rupture of ALA is associated with a high mortality rate.<sup>13</sup> In the 4 patients with ruptured abscess in the present series the diagnosis was only made intraoperatively. The doubt as to the cause of the peritonitis necessitated an operative approach. There is a paucity of papers reporting on non-operative management of intraperitoneally ruptured ALA in the literature, and the few papers that do have small numbers of patients.<sup>14</sup> These patients present with peritonitis and, unless the diagnosis of ALA is established before the development of peritonitis, the diagnosis is not uppermost in the clinicians' minds. Until there are large prospective studies that produce convincing evidence of successful non-operative management we will continue to advocate operative management of intraperitoneally ruptured ALA.

A liver afflicted by amoebic abscess is capable of nearly complete regeneration provided it is treated effectively.<sup>15</sup> The abscess cavity persists for a long time after clinical cure and hence clinical improvement does not correlate with the ultrasonographic resolution of the cavity.<sup>16</sup> We subscribe to the view that clinical criteria are a reliable method to assess cure and we do not share the view of Akgun *et al.*<sup>4</sup> that all patients be followed up with ultrasound examination to establish persistent cavities and response to treatment.

With early diagnosis and treatment the mortality of uncomplicated ALA is less than 1%.<sup>11</sup> The mortality rate in the present study was 0%.<sup>11</sup> Mortality rates for rupture into the peritoneum, chest and pericardium are 17 - 75%,<sup>2,8</sup> 6 - 36%<sup>2,17</sup> and 30%<sup>2</sup> respectively. The mortality rate for intraperitoneal rupture in this series was 25%.

The present study shows that aspiration can be confined to a small number of people who do not improve on treatment. We agree with Frey *et al.*<sup>5</sup> that aspiration of ALA should be limited to patients in whom pyogenic infection or secondary infection of an ALA cannot be ruled out or those in whom treatment over 48 hours with metronidazole has failed. Evidence that percutaneous aspiration or surgical drainage speeds resolution of ALA is lacking, but can be explained by comparison of treatments of abscesses of comparable size.<sup>5</sup>





Our findings confirm that medical management alone is effective for over 80% of patients with ALA. We have shown that lack of clinical improvement after 48 hours is the major criterion for aspiration, which should be ultrasound-guided, and that the size, site and surface proximity are not absolute indications for aspiration. This approach is safe and can be complemented by catheter drainage in selected cases, sparing patients the unnecessary morbidity of laparotomy. It is our recommendation therefore that all patients with ALA should initially receive medical management and that percutaneous aspiration should only be resorted to in case of failure of clinical improvement. Operative drainage should be reserved for intraperitoneal rupture.

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## An epidemiological perspective of substance use among high school pupils in rural KwaZulu-Natal

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**Objectives.** To investigate prevalence and the factors influencing substance use among rural high school pupils in KwaZulu-Natal in order to develop and implement intervention programmes.

**Design.** Cross-sectional study.

**Setting.** Twenty-eight high schools in southern KwaZulu-Natal.

**Subjects.** One thousand three hundred and eighteen grade 10 pupils.

**Outcome measures.** An anonymous self-reporting questionnaire was used to investigate the use of alcohol, tobacco (cigarettes), cannabis and solvents.

**Results.** Of the male scholars, 52.9% (95% confidence interval (CI): 45.4 - 60.3) reported ever using alcohol, 16.9% (CI: 11.5 - 24.0) reported using cannabis, and 13.1% (CI: 7.2 - 22.5) had

smoked more than one cigarette daily. Among male pupils 45.5% (CI: 38.6 - 52.6) had inhaled benzene and 34.6% (CI: 28.0 - 41.8), thinners; 7.4% (CI: 3.4 - 15.2) had used cocaine and 4.1% (CI: 1.0 - 10.6), crack. Female pupils reported significantly less use of alcohol (25.5%, CI: 17.6 - 35.3), cannabis (2.3%, CI: 1.3 - 4.1), cigarettes (more than one daily) (2.0%, CI: 1.0 - 4.1), and inhalation of benzene (18.8%, CI: 13.8 - 25.2) and thinners (10.8%, CI: 7.2 - 16). Logistical regression indicated that the odds of smoking cigarettes increased significantly ( $p < 0.0005$ ) with use of the other substances.

**Conclusion.** The results of this study confirm the prevalence of multi-substance use among pupils at the majority of rural high schools in this district and the need for targeted interventions to reduce/prevent this.

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