International Journal of Biomedical Research
ISSN: 0976-9633 (Online); 2455-0566 (Print)
Journal DOI: 10.7439/ijbr
CODEN: IJBRFA

Original Research Article

Treatment of liver abscesses: A prospective randomised trial

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Abstract

Background: The aim of the study was to evaluate the clinical presentation, and to investigate the effectiveness of continuous catheter drainage in comparison to needle aspiration in the treatment of liver abscesses.
Methods: This is a prospective randomized comparative study of 60 patients, presented in outpatient and emergency department at the hospital, randomized equally into two groups, percutaneous needle aspiration and pigtail catheter drainage. The effectiveness of either treatment was measured in terms of duration of hospital stay, days to achieve clinical improvement, 50% reduction in abscess cavity size and total/near total resolution of abscess cavity. Independent t-test was used to analyze these parameters.
Results: The success rate was significantly better in catheter drainage group (P=0.006). The patients in pigtail catheter drainage group showed earlier clinical improvement (P=0.039) and 50% decrease in abscess cavity volume (P=0.000) as compared to those who underwent percutaneous needle aspiration.
Conclusion: Percutaneous catheter drainage is a better modality as compared to percutaneous needle aspiration especially in larger abscesses which are partially liquefied or with thick pus.
Keywords: Liver abscess, catheter drainage, needle aspiration.

1. Introduction

A liver abscess is a suppurative cavity in the liver resulting from the invasion and multiplication of microorganisms, entering directly from an injury through the blood vessels or by the way of the biliary ductal system. Liver abscesses are most commonly due to pyogenic, amoebic or mixed infections. Pyogenic abscesses account for almost 80% of all liver abscesses in the developed world and are most often.

Liver abscess has been recognized since Hippocrates (circa 400 B.C.) who speculated that the prognoses of the patients were related to the type of fluid within the abscess cavity [1]. Although amoebic liver abscess occurs more commonly on a worldwide basis, the pyogenic liver abscess predominates in the United States. The aetiology of these abscesses has changed over the last few decades. Historically, the commonest cause had been acute appendicitis but, with evolution and advancement of surgical practice and microbiology over time, its frequency as the primary source of abscess has decreased. In contrast, the increasing frequency of cholelithiasis and biliary tract pathology, with their potential to incite ascending portal sepsis, has replaced appendicitis.

Liver abscess is found more commonly in men between 20 and 40 years of age, but can occur at any age. Approximately 60% are solitary and mainly located in the right lobe of the liver, as a result of the streaming of portal blood flow secondary to the fact that the right lobe is predominantly supplied by the superior mesenteric vein, and because most of the hepatic volume is in the right lobe. When multiple abscesses are present, pyogenic or mixed is the most probable type. Patients usually present with a constant dull pain in the right upper quadrant of the abdomen which may be referred to the scapular region or the right shoulder. These patients usually have fever of between 38^{o}C and 40^{o}C.

Liver abscesses, both amoebic and pyogenic, continue to be an important cause of morbidity and mortality in tropical countries. However, recent advances in interventional radiology, intensive care, progress in antibiotic therapy, and liberal use of sonography and computerized tomography scanning of the abdomen have

led to early diagnosis and treatment of patients with liver abscess, thus improving the patient outcome. Percutaneous drainage of liver abscess under USG guidance has been an important advancement in the treatment of pyogenic liver abscesses.

The primary mode of treatment of amoebic liver abscess is medical; however as many as 15-20 % of amoebic abscesses may be refractory to medical therapy [2]. Also, secondary bacterial infection may complicate 15-25 % of amoebic liver abscesses [3]. In such patients and in patients with pyogenic liver abscesses, surgical drainage has been the traditional mode of treatment [4]. However, operative drainage is associated with significant (10-50 %) morbidity and mortality [5].

In recent years, image-guided percutaneous drainage has been increasingly used to treat liver abscesses with reported success rates ranging from 70-100% [6-8]. Although percutaneous placement of an indwelling catheter is the method most widely preferred to drain liver abscesses [9], recent studies have claimed needle aspiration to be a simpler, less costly, and equally effective mode of treatment [10,11].

2. Materials and methods

2.1 Study design

This is a prospective randomized comparative study conducted by the Department of Surgery in SBKS MI&RC. A total of 60 patients were included in the study, randomized into two groups; percutaneous needle aspiration (PNA) (n=30) and pigtail catheter drainage (PCD) (n=30). The patients were studied from July 2012 till April 2013.

2.2 Participants

The patients were selected from those attending the outpatient department only at the hospital. The age of patients varied from 15 to 60 years with most of the patients falling within the range from 31-40 years. All the patients diagnosed to have liver abscess clinically and radiologically [on ultrasonography (USG) and/or CT scan] were included in the study. Exclusion criteria were: all abscess cavities smaller than 5 cm in their greatest dimension, prior intervention, ruptured liver abscess, uncertain diagnosis, concomitant biliary tract malignancy and uncorrectable coagulopathy.

2.3 Methods

Detailed history and clinical examination was done. Laboratory and imaging investigations included complete haemogram; liver function tests; prothrombin time; international normalized ratio; activated partial thromboplastin time; blood culture; amoebic serology; imaging-CXR; abdominal USG with or without CT scan of the abdomen; and other investigations as per specific indications in different patients.

An informed consent was obtained from the participating patients and all the consenting patients were started on medical treatment as per our protocol.

All the patients empirically received injection Metronidazole 1 gm IV every 8 hourly, injection Ceftriaxone 1 gm IV 12 hourly, injection Amikacin 500 mg IV 12 hourly. The empirical treatment was revised based on the culture and sensitivity report. However, patients in whom pus culture was sterile continued on the same treatment. The antibiotics and metronidazole were given for duration of 10 and 14 days respectively.

The two sets of random numbers generated were assigned to the two intervention groups. Once a participating subject gave valid consent the pre-determined intervention was carried out as follows: The percutaneous procedures were carried out under local anesthesia (2% lignocaine) with IV analgesic and sedation if required. The procedures were carried out under USG guidance.

2.4 Percutaneous Needle Aspiration (PNA)

The patient was subjected to USG of the abdomen and the characteristics of the abscess cavity(ies) were recorded. Local anesthesia was infiltrated at the proposed puncture site using a 23 G needle. Under USG guidance and using 18 G spinal needle the abscess cavity was entered and pus was aspirated till no more pus could be aspirated further. A sample of pus was sent for Gram stain, culture, sensitivity and wet mount for *Entamoeba histolytica* trophozoites. A dressing was applied at the needle puncture site.

2.5 Pigtail Catheter Drainage (PCD)

The PCD was accomplished by placing a 12-French pigtail catheter in the abscess cavity under USG guidance. The patient was subjected to USG of the abdomen and the characteristics of the abscess cavity (ies) were recorded. Local anesthetic was infiltrated in the proposed area of puncture. Using a No.11 blade a small stab was made on the anesthetized skin. A percutaneous pigtail catheter set with a 12 French catheter was used for drainage. Under USG guidance the initial puncture needle was inserted through the skin stab and guided to the center of the abscess cavity. The stillate was taken out and pus was aspirated to reconfirm the position and the aspirated pus was sent to the lab for testing. A 0.038” straight tip guide wire was inserted through the needle and the needle was taken out without displacing the guide wire. The tract was dilated with plastic dilators serially up to 12 French size. The 12-French pigtail catheter was then passed over the guide wire which was taken out, and the catheter was fixed to the skin using 1-0 Silk suture. The catheter was attached to a collecting bag via the supplied connector.

2.6 Evaluation of the response to intervention

The clinical response (temperature) and laboratory parameters [total leukocyte count (TLC), liver function test (LFT), etc.] were recorded on a daily basis. In the patients undergoing PNA, USG was repeated after a gap of two days and aspiration repeated if the cavity size was still found to be greater than 5 cm. The same procedure was repeated after a gap of another two days and aspiration repeated if needed.

The failure of clinical improvement in terms of fever, abdominal pain and tenderness and leukocytosis or decrease in size of the abscess cavity after the third attempt of aspiration was taken as failure of needle aspiration. These patients underwent PCD but were not added to the PCD group.

In patients who underwent PCD, besides recording the clinical and laboratory parameters of the patient every day, daily output of the catheter was measured and the catheter was flushed with 10 cc of normal saline (this volume was deducted from the total drainage). A decision to remove the pigtail catheter was made when the total drainage from the catheter decreased to less than 10 mL/24 h for two consecutive days. The patient was administered Tab. Diloxanide Furoate 500 mg post procedure twice a day for 10 days at the time of discharge.

2.7 Follow up

The patients were followed up weekly for a month, monthly for three months and at the end of six months, for clinical evaluation and USG assessment of abscess cavity until complete resolution of the abscesses was achieved. Data was collected and recorded in the printed proforma by the investigator.

3. Results

A total of 60 patients randomized into two groups of 30 each were included in the study. The following observations were made:

3.1 General characteristics

The age of the patients varied from 15 years to 60 years with most of the patients falling within the age range from 31-40 years (22 patients). The second most common age group was 21-30 years (18 patients) and the number of patients was less in extremes of age. There were 50 male and 10 female patients with liver abscess involved in the study. The male to female ratio was 5:1.

3.2 Symptoms and signs

It was observed that anorexia and pain in the right upper quadrant of the abdomen was the most common symptoms. Weakness and fever were other frequently presenting symptoms. Approximately half of the patients had symptoms of, weight loss and night sweats. Pain in the right shoulder region and cough were present in some of the patients. Only 10% of the patients gave a history of diarrhoea prior to illness (Table 1). In this study, hepatomegaly was found to be present in 50 of 60 patients whereas pleural effusion was found in 4 of 60 patients.

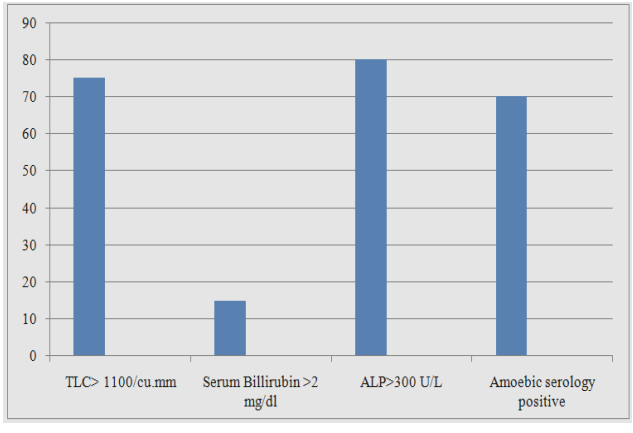
Table 1: Symptoms and signs

Symptoms	Number of Patients	Percentage (%)
Anorexia	60	100
Right upper quadrant pain	57	95
Weakness	56	93
Fever	54	90
Weight loss	30	50
Night Sweats	30	50
Nausea/vomiting	20	33
Chills	15	25
Cough	14	23
Right Shoulder Pain	12	20
Diarrhoea	6	10
Dypsnoea	3	5

3.3 Laboratory data

It was observed that 45 of 60 (75%) patients had leukocytosis. Elevation of serum alkaline phosphatase was also observed in 80% of the patients. Amoebic serology positivity (>0.90, EIA) was found in 70% of the patients (Figure 1).

Figure 1: Laboratory data



3.4 Pus culture

Pus aspirated from all abscesses was sent for culture and sensitivity. Cultures were found to be positive in 20 of 60 (33%) of the cases. The rest were sterile.

3.5 Microbiology

Among the pus culture positive cases *Escherichia coli* was isolated most frequently i.e. 10 of 20 culture positive patients. It is followed by *Klebsiella* spp. which was isolated in 8 cases. *Pseudomonas* spp. and *Staphyloccocus aureus* were isolated in 1 patient each (Table 2).

Table 2:- Culture Positive microbiology

Microbiology	Number	Percentage (%)
Number of growth	20	33
Klebsiella spp.	8	13.33
E. Coli	10	16.67
Pseudomonas spp.	1	1.67
S. aureus	1	1.67

3.6 Type of abscess

Amoebic liver abscesses were encountered more frequently (60%) compared to pyogenic (22%), amoebic abscesses with secondary bacterial infection (8%) and abscesses of indeterminate etiology (10%) (Table 3A & 3B).

Table 3A: Etiological Types

Etiology	Amoebic Serology Result	Pus Culture Result
Amoebic	+	-
Pyogenic	-	+
Amoebic with secondary infection	+	+
Indeterminate	-	-

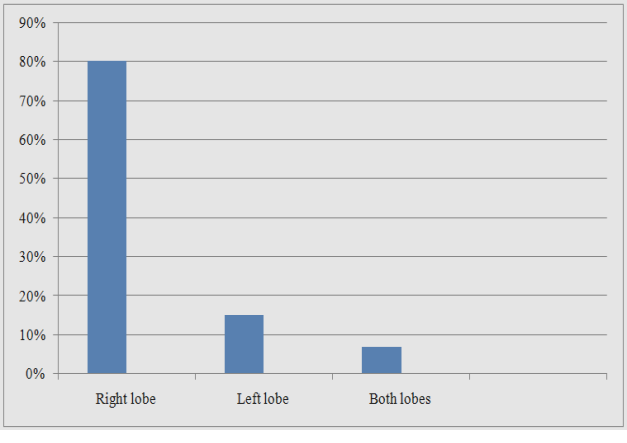
Table 3B: Type of abscesses in each group

	Amoebic	Pyogenic	Mixed	Inderminate
PNA	18	6	2	4
PCD	18	7	3	2

3.7 Location of the abscess

The majority 80% of the abscesses were located in the right lobe of liver, 15% in the left and 5% in both lobes (Figure 2).

Figure 2: Location of the abscess



3.7 Number of abscess

Three quarters of the cases studied were found to have solitary liver abscess cavity, whereas the rest of the patients had multiple abscesses.

3.8 Volume of the abscess

It was observed that the volume of the abscess cavities was mostly between 100-400 mL (Table 4).

Table 4: Volume of the abscess

Volume of cavity (in ml)	Number of Patients
51-100	1
101-150	6
151-200	10
201-250	12
251-300	10
301-350	11
351-400	4
401-450	1
451-500	1
501-550	1
551-600	2
601-650	0
651-700	0
701-750	0
751-800	1

3.9 Interventions and their results

A total of 60 patients underwent either of the two percutaneous procedures randomly and their response to treatment was recorded and analyzed (Table 5). Pigtail percutaneous drainage was successful in all the 30 cases. On the other hand, image-guided needle aspiration was successful only in 24 of 30 patients (P=0.006). Out of these 24 patients successfully treated, 10 patients required only one aspiration, 10 required two aspirations, and 4 required three aspirations. The 6 patients who did not show clinical improvement and / or decrease in cavity size despite 3 aspirations were taken as failures. In the PNA group, on comparing the cavity volumes the mean cavity volume in those who were successfully treated was 201.4 cc which was significantly less than those failing treatment; the mean volume being 403.6 cc (P<0.011). The patients in PCD group showed earlier clinical improvement (P=0.039) and 50% decrease in abscess cavity volume (P=0.000) as compared to those who underwent PNA. However, there was no significant difference between the duration of hospital stay or the time required for total or near-total resolution of cavity.

Table 5: Results

Treatment Group					
Parameter	**PCD (n=30)**		**PNA (n=30)**		**P Value**
	Number of Patients	**Mean±SD**	**Number of Patients**	**Mean±SD**	
Volume of largest cavity (in ml)	30	98-770 302±122	30	118-572 249±121	0.096
Success	30	100%	24	80%	0.006
Hospital stay (in days)	30	6-24 11.3±3.8	30	5-21 10.5±5.2	0.501
Clinical improvement	30	3-9 4.5±1.55	24	2-9 5.5±1.9	0.039
Time for 50% reduction in cavity size (in days)	30	3-9 4.9±1.6	30	4-10 7.1±2.3	0.000
Time for total or near total resolution of cavity (in weeks)	30	8-24 10.9±4.1	30	8-24 10.1±4.2	0.454

4. Discussion

Liver abscess is a major tropical disease of the gastrointestinal system [12,13]. The liver abscess is mainly classified into amoebic and pyogenic. Pyogenic liver abscess which used to be mainly tropical in location is now more common due to increased biliary interventions, stenting, A total of 60 patients underwent either of the two cholecystitis, cholangitis etc. In our study we found the male to female ratio to be 5: 1. The most frequently affected age group was in the third and fourth decade.

The common symptoms and signs of liver abscess in our study were anorexia, right upper quadrant pain and tenderness and hepatomegaly (80%).

In our study, 80% of the abscesses were located in the right lobe of liver and 78% of our patients had solitary abscesses. We encountered multiple liver abscesses in 22% of the patients, similar to the 20-25% incidence of multiple liver abscesses reported by Sharma *et al* [14].

The type of abscess was determined on the basis of amoebic serology and pus culture reports [15]. In our study we found 60% of the abscesses to be amoebic in etiology, 22% to be pyogenic, 10% to be indeterminate and 8% to be amoebic with secondary bacterial infection (or mixed liver abscess, MLA). Khan *et al* in their series reported 68% amoebic, 21% pyogenic, 8% indeterminate, and 3% MLA [15]. The use of serological testing for diagnosis of amoebic liver abscesses can occasionally lead to either false negative results early in the course of the disease, due to delay in rise of antibody titre , or to false positives due to background subclinical amoebic infections. Consideration of high titres for diagnosis may help exclude these false positives [16].

The pus cultures were negative in 40 of 60 patients. Aerobic cultures were declared negative after 48 hours of incubation. As several of our patients prior to reporting to our hospital had been given antibiotics as well as antiamoebic drugs, this might explain the finding of 10% cases with indeterminate etiology. Similar experience has been reported by other researchers as well [15].

The most frequently isolated bacteria on pus culture was *Escherichia coli* (16.67%) closely followed by *Klebsiella* species (13.33%). *Escherichia coli* has been reported to be the organism most frequently grown in western series [8,17]. However, Asian series have reported *Klebsiella* to be the most frequently isolated bacteria [18-20].

We performed image-guided percutaneous intervention in 60 patients with uncomplicated liver abscess and obtained good results. There was no mortality or any major complication requiring any treatment. Several researchers have employed both the modalities, i.e. PNA as well as PCD with varying degrees of success. Several groups have documented that significant number of patients can be managed with a combination of systemic antibiotics and percutaneous drainage with excellent results [21-23].

Many solitary and some carefully selected macroscopic multiple abscesses are underwent to percutaneous abscess drainage. Surgical drainage is usually reserved for patients who have failed percutaneous drainage, those who require surgery for management of underlying problems and some patients with multiple macroscopic abscesses [24].

Several groups have reported reasonably good results with PNA along with systemic antibiotics [11,22]. Giorgio *et al* performed on an average 2.2 aspirations in 115 patients and reported resolution of symptoms and hepatic lesions in 98% of the patients. In our study we treated 30 patients with PNA along with systemic antibiotics. Of these 30 patients, 24 were successfully treated with 10 requiring, only one aspiration, 10 requiring a second aspiration and 4 patients requiring a third aspiration as well. 6 of these 30 patients failed to improve

clinically and did not show significant decrease in abscess cavity even after 3 aspirations. Thus, 24 patients who were successfully treated with aspiration required an average of 1.8 aspirations. The mean duration of time taken for clinical improvement was 5.5±1.9 days in this modality of treatment. Rajak *et al* [25] reported a success rate of 60% with needle aspiration. However, in their study only two attempts of aspiration were made and failure to attain clinical, hematological and radiological improvement was taken as failure of therapy.

Of 6 patients who did not respond to PNA, 4 improved on PCD and 2 was lost to follow up. But these patients were not included in the PCD group as success. Of these 6 patients, 3 were amoebic, 3 were pyogenic and out of these 3 pyogenic abscesses, *Escherichia coli* was seen in 2 and *Klebsiella* in 1 patients.

It can be said that in recent years image-guided percutaneous treatment (needle aspiration or catheter drainage) has replaced surgical intervention as the primary treatment for liver abscess [6-9,26,27].

The major advantages of PNA over PCD are: 1) it is less invasive and less expensive; 2) avoids problems related to catheter care; and 3) multiple abscess cavities can be aspirated easier in the same setting [10,11]. However, in our study we had a success rate which was significantly lower than with catheter drainage (80% versus 100%, P=0.006). There are some problems with catheter drainage like nuisance to the patient, pain, cellulites at the insertion site and sometimes catheter dislodgement.

The success rate of PNA in the literature varies from 75-100% [10,28]. The success rate in our study after single aspiration was 33%, after second aspiration 66% and after third aspiration it was 80%. Although, needle aspiration is a much simpler procedure when compared to catheter drainage repeated procedures are quite unpleasant and traumatic for the patients and may not be acceptable to many. Even after repeated aspirations the success rate was far from being 100%. Therefore, those patients who failed after a third aspiration attempt were offered catheter drainage.

The average size of abscess in our study was 302±122 mL and 249±121 mL for the PCD and PNA group respectively, comparable to the study reported by Rajak *et al* (335 mL and 221 mL respectively) [25]. The success rate achieved by Rajak *et al* was 60%, comparable to the success rate after the second aspiration in our study, i.e. 66%. Subsequent aspirations seem to improve the success rate of therapy.

In contrast to some of the earlier reports that show that the initial size of the abscess cavity did not affect the ultimate outcome [11,22], larger abscesses are more difficult to evacuate completely in one attempt, necessitating subsequent aspirations [25]. The average volume of the 6 patients in whom PNA failed was significantly larger than the average volume of the patients who could be successfully treated with PNA (403.6 mL and 201.4 mL respectively, P=0.011).

Another important reason for failure of needle aspiration is the inability to completely evacuate the thick viscous pus that may be present in some of the abscesses. Rapid re-accumulation of pus in the abscess is another reason described for failure of needle aspiration [28].

Placement of an indwelling drainage catheter addresses all three of these issues as it provides continuous drainage, drains thick pus because of wider caliber catheter, and prevents re-accumulation. This explains the higher success rates (100%) observed in our study and several previous studies [10,25,26,29].

The only reasons for failure of PCD as reported in some of the earlier series [30,31] have been either thick pus not amenable to percutaneous drainage (this can be overcome by placement of a wider bore catheter) or premature removal of drainage catheter. No recurrence occurred in any of our cases during the follow up period. However, both treatment modalities resulted in rapid clinical relief with most patients showing resolution of signs and symptoms within the first 4 days of the procedure.

The time required for 50% reduction in the cavity size was significantly less in the PCD compared to PNA group (4.9 days and 7.1 days respectively, P=0.000). However, time required for total or near-total resolution of the abscess cavity did not show any significant difference in the two groups (PCD=10.9 weeks, PNA=10.1 weeks, P=0.454). It can be concluded that the abscess cavities showed faster collapse during the initial period in the PCD group but it did not have an advantage as far as total or near-total resolution of cavity is concerned. Similar observations were recorded by other investigators as well [9,25].

Complications such as hemorrhage, pleural effusion/empyema, persistent bile drainage, catheter displacement, sepsis etc., have been reported with both PNA 4% in [10] and PCD 12% [23]. Baek *et al* and Giorgio *et al* described the much lower incidence of complications with PNA than with PCD as one of the major advantages of needle aspiration over catheter drainage. However, in our study and some recent studies [25,32], both the procedures were found to be safe if performed properly with minimal complications. There was no mortality in either of the study groups.

Singh and Kashyap [9] reported a 15% incidence of secondary bacterial contamination after repeated needle aspirations; however, others [10,11,25] have not encountered this problem. Although secondary bacterial

infection remains a possibility with indwelling drainage catheters this complication has been rarely reported in liver abscess [7].

One limitation of our study is that the etiology of abscess was not uniform and formed a heterogeneous group with abscesses of both amoebic and pyogenic etiology existing in both groups. Also, about 10% of the abscesses were of indeterminate etiology. Anaerobic culture was not performed and no studies to detect fungus were done.

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