

# A Comparative Prospective Study of Characteristics and Associated Morbidity in Culture Positive Liver Abscess (CPLA) with Culture Negative Liver Abscess (CNLA)

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**Abstract:** *Background:* There are limited studies focusing on liver abscess with negative microbiological cultures. This study evaluated the clinical and prognostic differences of patients with culture-negative liver abscess (CNLA) compared to those with a positive culture (CPLA) and compared these factors between *K. pneumoniae* liver abscess (KLA) and *E. coli* liver abscess (ELA). *Methods:* A prospective study of the patients who admitted with a liver abscess at tertiary care hospital at SMIMER medical college and municipal hospital, surat from November 19' to april 21'. *Results:* Among a total of 19 patients with liver abscess, 30.50% had positive cultures. *K. pneumoniae* (n = 36) was the most common cause, followed by *E. coli* (n = 16). Patients with CPLA were significantly older (p = 0.07) and more frequently had cholelithiasis or biliary tract disease (p = 0.03) compared to patients with CNLA. In-hospital mortality (p = 0.01) and recurrence (p = 0.07) were no different between the two groups. The length of hospital stay was significantly longer in patients with CPLA (p = 0.03) compared with those with CNLA. *Conclusions:* Our study suggests that prognosis including presentation as sepsis and recurrence rates were no different in CNLA and CPLA group however Metastatic infections and in hospital mortality were significantly higher and CPLA group compared to CNLA group. Clinical parameters and laboratory parameters were different between both CNLA and CPLA groups and mean hospital stay was higher in CPLA group compared to CNLA group.

**Keywords:** Liver abscess, Culture-negative, *E. coli*, *K. pneumoniae*

## 1. Introduction

Pyogenic liver abscess is a common intra-abdominal infection seen in our country and is a life threatening disease. A pyogenic abscess is defined as a collection of pus consisting of numerous inflammatory cells. Infection is associated with necrosis from inflammation of surrounding tissue.<sup>[1]</sup>

In the early 1900s, the most common cause of HA was pylephlebitis secondary to appendicitis<sup>[2]</sup>. In the late 1900s, biliary tract disease emerged as the most frequent culprit<sup>[2, 3]</sup> and it remains the most common cause of HA today.<sup>[3, 5, 6, 7]</sup> recently, there has been an increase in the incidence of HA arising in association with malignancies and their treatment, including HA from liver metastasis<sup>[4, 8]</sup> and as complications of transarterial chemoembolization (TACE) or radiofrequency ablation (RFA).<sup>[9-12]</sup>

The etiology of HA can be bacterial, parasitic (amebic essentially), mixed (pyogenic superinfection of parasitic abscess) or more rarely fungal.<sup>[2]</sup>

The exact pathogenesis of a pyogenic liver abscess is unclear; however several mechanisms of infection have been discussed.

- 1) Transportation of virulent organism through the portal system from the gastro intestinal track.
- 2) Spread if infection from the billiary tract.
- 3) Blood-borne infection via the hepatic artery.
- 4) Extension from a contiguous disease process.
- 5) Trauma due to blunt or penetrating injury.
- 6) Cryptogenic.

The source of infection usually arises from the biliary, intestinal tract or portal system. Blood cultures are an important adjunct to the diagnosis of pyogenic liver abscess and although their yield is usually lower than pus aspirate of liver abscess done through needle aspiration, they may provide helpful information in patients before they receive antimicrobials or aspiration of their abscess. It is preferred to perform a blood culture for patient with liver abscess at the time of admission.<sup>[1]</sup>

There are challenges in defining the different microbiological pathogens. One reason for this problem is that it is common that pus from a liver abscess is collected after administration of antibiotics.<sup>[1]</sup>

The best treatment for liver abscess is infection control by drainage and administration of intravenous antibiotics that cover etiologically causative organism obtained through culture and sensitivity report. Empirically, 3rd-generation cephalosporins plus metronidazole or  $\beta$ -lactam/ $\beta$ -lactamase inhibitor are recommended initially, and antibiotics should later to be changed based on culture and antimicrobial susceptibility data. Treatment has shifted towards imaging guided percutaneous needle aspiration or percutaneous catheter drainage which reduces chances of surgical exploration for liver abscess. However, surgical intervention is only indicated for ruptured liver abscess with peritonitis.<sup>[1]</sup>

There is uncertainty regarding management of culture negative liver abscess (CNLA). It remains unclear what kind of empiric antibiotics work better for CNLA patients. It is unclear whether the prognosis like metastatic infection or mortality in CNLA patients is similar to that with culture proven patients.<sup>[13]</sup>

## 2. Methods

**Study Design:** This prospective study was conducted at SMIMER medical college and general hospital the tertiary hospital from November 19' to april 21'.

### Patients and Definitions:

All patients with confirmed diagnoses of liver abscess based upon inclusion criteria who were admitted in smimer, Surat between November 19' to April 21' were considered as study participants. Sample size was calculated considering the proportion of liver abscess cases out of total admitted cases in last 6 months from the data records of the Department of Surgery at 3° care hospital is 7.75%. Patients willing to give consent. All hospitalized patients > 18 years and <65 years old who were admitted to this hospital diagnosed with liver abscess. Microbiologic data were collected from at least 1 set of blood cultures obtained prior to starting antibiotics. Microbiologic data were collected from pus obtained through an invasive procedure including usg guided aspiration / Pigtail insertion prior to starting antibiotics. Patients below the Age of 18 years and more than 65 years were excluded. Other excluded patients were pregnant women, patients to whom antibiotics were already started prior to obtaining blood culture or pus through invasive procedure, Patients with Altered coagulation profile/bleeding tendencies and Known case of liver abscess in past or recurrent liver abscesses.

### Data Collection:

The following data were collected: age, sex, underlying disease, laboratory findings, microbiologic data, treatment strategy, complications, and clinical outcomes. Inhospital mortality was used as the main outcome for assessing mortality in patients with a liver abscess. Data were collected To Evaluate the clinical and prognostic difference in patients with culture negative liver abscess-CNLA compared to that with positive Microbiological culture in terms of parameters like clinical and laboratory parameters, need of invasive procedure, Metastatic infection, in hospital mortality, length of hospital stay, recurrence.

### Ethical approval:

The Institutional Ethical Committee (IEC) of the SMIMER medical college and municipal hospital approved this study.

### Statistical Analysis:

The independent sample t-test was used to analyze continuous variables, and the Chi-square test was used for categorical variables and a p-value of < 0.05 was considered statistically significant.

## 3. Results

**Demographic Data:** The mean age of the study group is 44.78 years with youngest patient is of 20 years and oldest patient is of 65 years. Commonest age group for liver abscess was 41-50 years (31.35%) followed by 51-60 years (27.11%).

Age Group	No. of Patients	%
	19	16.10
31-40	21	17.79
41-50	37	31.35
51-60	32	27.11
61-65	9	7.6

Liver abscess was commonest in male patients with 85.59% and in female patients 15.45%.

Sex	No. of Patients	%
Male	101	85.59
Female	17	15.45

**Microbiological Data and Laboratory parameters:** In this study 105 patients in total were subjected to invasive treatment in which microbiological data were obtained through aspirated pus through the cavity. In rest of the 13 patients that were treated conservatively in which microbiological data were obtained through blood culture prior starting the antibiotics. Out of which 36 patients came out positive for pyogenic organism and 82 patients did not show any growth. Out of 36 culture positive liver abscesses E. coli was the commonest etiological organism seen in n=16 patients (44.44%) followed by which klebsiella n=10 (27.11%) was observed.

Culture Report	No. of Patients	%
Culture Positive	36	30.50
Culture Negative	82	69.49

	CPLA (n)	CPLA in %	CNLA (n)	CNLA in %
Blood Culture	1	2.8	12	14.63
Pus Culture	35	97.22	70	85.36

Organism	No. of Patients	%
E. Coli	16	44.44
Klebsiella	10	27.77
S. Aureus	7	19.44
Pseudomonas	3	8.33

In CPLA patients low Hb <10mg/dl was observed in 30.55% (n=11) of the patients and 25.60% (n=21) of the CNLA patients. Total counts >15, 000/cumm in 63.88% (n=23) in CPLA and 28.04% (n=23) in CNLA patients was seen. Altered renal function with S. Creatinine >1.6 mg/dl was seen in 8.33% (n=3) in CPLA patients and NIL is CNLA patients. Raised total bilirubin >2.5 mg/dl was seen in 19.44% (n=7) in CPLA and 12.19% (n=10) in CNLA patients and raised ALP >140mg/dl was seen in 25% (n=9) of CPLA and 31.70% (n=26) of CNLA patients.

	CPLA	CPLA in %	CNLA	CNLA in %
HB <10mg/dl	11	30.55	21	25.60
TC >15, 000/cumm	23	63.88	23	28.04
PLT <1 lakh/cumm	4	11.11	2	2.4
Billirubin >2.5mg/dl	7	19.44	10	12.19
Raised ALP >140mg/dl	9	25.0	26	31.70
S Creatinine >1.6mg/dl	3	8.33	0	0

In culture positive patients the commonest symptom was abdominal pain observed in 88.88% of the patients followed by fever observed in 86.11% patients. Similarly in culture negative patients the commonest symptom was fever seen in

79.26% of the patients followed by fever seen in 59.75% of the patients.

Symptoms	CPLA	CPLA (%)	CNLA	CNLA (%)
Fever	31	86.11	49	59.75
Abdominal Pain	32	88.88	65	79.26
Jaundice	11	30.55	10	12.19
Diarrhoea	6	8.33	36	43.90

In culture positive patients sepsis was observed in 18.75% of the patients and in culture negative patients it was seen in 10.97% of the patients (P value=0.07). In culture positive patients biliary tree disease including cholelithiasis and choledocholithiasis was evident in 19.44% of the patients compared to 4.87% patients of culture negative patient. (P value=0.03). Similarly in culture positive patients associated liver paranchymal disease was seen in 4.87% of the patients compared to that of 1.2% in culture negative patients (P=0.008). Metastatic infection was seen in 2 patients in form of pelvic abscess in CPLA patients and in 1 patient in form of appendicular abscess in CNLA patients (P value=0.01). In hospital mortality was observed in 5.55% (n=2) in CPLA patients compared to 1.21% (n=1) in that of CNLA (P value=0.01). All three patients with mortality presented in septic shock due to intra peritoneal rupture of liver abscess on admission with features of severe Hypotension and went through exploratory laparotomy. Follow up was obtained after 1 month of all patients to analyse the recurrence which was observed in 8.3% (n=3) patients of CPLA compared to 6.09% (n=5) of CNLA patients. (P value: 0.07).

	CPLA	CPLA in %	CNLA	CNLA in %
Presentation as sepsis	6	18.75	9	10.97
ICU admissions	10	27.77	9	10.97
Metastatic infections	2	5.55	1	1.21
Length of hospital stay (Mean)	7.8		5.3	
In hospital mortality	2	5.55	1	1.21
Recurrence	3	8.3	5	6.09

#### 4. Discussion

In 1938, Oschner's classic review heralded surgical drainage as the definitive therapy. Infection remained unchanged. Untreated the infection remains unevenly fatal. India being the tropical country, 400 million harboring *E. histolytica*, the causative organism of liver abscess, it is of immense importance for understanding the same. The rising incidence in alcoholics, immunocompromised individuals has a matter of grave concern and the complication rates are high in these patients. The changing pattern of incidence, diagnostic modalities, treatment and complications, rising incidence in alcoholics and immunocompromised individuals this is current serious problem in our country. 70% of the people are in the rural area and therefore it mandates, appropriate and realistic guidelines to be drawn for early diagnosis and for the change in management strategies, to reduce the morbidity and mortality associated with it.

The epidemiologic profile of liver abscess differs between countries. *E. coli* was a prevalent cause of liver abscess until the mid-1980s; however, since then, *K. pneumoniae* has

become increasingly important as a liver abscess pathogen [15]

However, there are few data on the clinical characteristics and prognosis for liver abscess with no etiologic organism identified or due to other pathogens.

The age of the patients varied between 20-65 years. The mean age was 44.78 years which is in accordance with studies like Sharma et al. which reported it to be 40.5. The highest incidence was noted in 41-50 years of age group with incidence of 31.75% as most of the patients in this age group were alcoholics followed by 51-60 years with incidence of 27.11% as most of patients had lower immunity and known case of chronic liver parenchymal disease. [15]

Indian data show predominant male involvement; Sharma et al. reported male to female ratio to be 7 : 1. However in our study it appears to be 5.3: 1 as alcoholic liver disease and liver paranchymal diseases were more observed in male patients. [15]

Our study demonstrated culture positivity in 30.50% (n=36) of the patients which were obtained through invasive procedure in 105 patients and via blood culture prior to starting antibiotics in 13 patients. Out of total 118 patients 82 patients showed no growth of any organism. Out of 13 patients went through the blood culture and 1 patient came positive for growth of *E. coli* and 12 patients showed no growth.

The epidemiologic profile of liver abscess differs between countries. *E. coli* was a prevalent cause of liver abscess until the mid-1980s; however, since then, *K. pneumoniae* has become increasingly important as a liver abscess pathogen [16, 17-19]. In our study *E. coli* was cultured most common organism 44.44% (n=16) followed by *Klebsiella* 27.77% (n=10) and other obtained organisms were *Pseudomonas aeruginosa* and *S. aureus*.

The frequency of Fever was 86.11% in CPLA where as 59.75% was seen in CNLA patients along with abdominal pain in 88.88% in CPLA and 79.75% in CNLA. These two symptoms were the most commonly presented in our study. In other study Sharma et al. [43] and Mukhopadhyay et al. [14] fever accounted for 67-87% of the patients and abdominal pain accounted to 62-94% of the patients. The onset of the disease is subjected to great variations depending upon the type, location and quantity of liver abscess; it may be acute, insidious, clinically undetectable or fulminant form. Duration of symptoms longer than 2 weeks is seen in 14-41% in different series. In a study of amoebic liver abscess by Amarapurkar and colleagues of 131 patients, the duration of symptoms less than 2 weeks was seen in 83.9% of cases as early drainage of the abscess was obtained by them. According to Maingot's abdominal operations, most patients of liver abscess manifest symptoms for less than 2 weeks but a more indolent course occurs in 1/3rd of the patients.

On analysis of the laboratory investigations 30.55% of the patients were anemic in CPLA and 25.60% were anemic in CNLA group of patients which was <10mg/dl. Alcoholics and patients with chronic liver disease along with female

patients accounted for the anemia in our study and one patient with occult colonic malignancy was anemic in our study. According to Bhagwansatiani and Eugene D. Davidson, anaemia was present in 39% of cases as one criteria they had selected more number of patients with history of alcoholism which had higher numbers of patients with alcoholic liver disease [20]. Leukocytosis was comparable to the same study as well.

Observations by BhagwanSatiani and Eugene D. Davidson revealed elevated serum bilirubin was seen in 36% of cases as there were more patients with alcoholic liver disease in that study, whereas in our study the elevated bilirubin levels were noted in 19.44% patients in CPLA and 12.19% patients in CNLA. [20] Raised ALP were noted in 25% patients in CPLA and 31.70% in CNLA patients and observations by BhagwanSatiani and Eugene D. Davidson increased levels of ALP was seen in 63% of cases. Raised billirubin and ALP levels were due to inflammatory changes in hepatic cells due to liver abscess leading to hepatitis and were due to mechanical billiary obstruction caused by abscess cavity. [20].

Surgical drainage of liver abscesses has been an accepted therapy for decades. The diagnosis and treatment of liver abscess has changed due to advances in imaging techniques. In current study out of 118 patients of liver abscesses 13 patients with volume <50cc were treated conservatively out of which 2.7% were of CPLA group compared to 14.63% of CNLA group. According to Hiroshi Okano, Katsuya Shraki percutaneous aspiration is not required in all cases of liver abscess. A subset of cases with small liver abscess < 300 cc can be successfully managed conservatively. In that study they had higher mortality rate as they had chosen to treat patients conservatively compared to our aggressive approach for invasive treatment which lead to significantly less mortality in our study [21]. In CPLA patients In CPLA patients 55.55% (n=20) patients were treated by USG guided aspiration and 25% (n=9) were treated by USG guided Percutaneous pigtail drain insertion and 16.66% (n=6) underwent exploratory laparotomy with peritoneal lavage due to intraparietoneal rupture of liver abscess. In CNLA 36.58% (n=30) patients were treated by USG guided aspiration and 40.24% (n=33) were treated by USG guided Percutaneous pigtail drain insertion and 8.53% (n=7) underwent exploratory laparotomy with peritoneal lavage due to intraparietoneal rupture of liver abscess. According to Antonia, Giorgio, Lucien Turuntino percutaneous needle aspiration is an efficient, effective and low cost technique that can even be performed on an out patient basis [22]. According to Arshed Zafar, However more aggressive treatment, the mortality rate remained 60-80%. The development of modern imaging techniques, advancement of drainage techniques, improved microbiological identification and the nutritional care decreased the mortality to 5-30%. Yet, the prevalence of Sajjad Ahnied, needle aspiration is safe, rapid effective method of treating liver abscess. Routine aspiration is not indicated. It should be initial line of treatment in abscess > 50 cc, impending rupture or abscess that do not respond to chemotherapy [23]

Pyogenic liver abscess is a potentially life-threatening infection with high mortality. However in our study 18.75%

patients in CPLA and 10.97% patients in CNLA presented with features of sepsis on admission and 27.77% patients in CPLA and 10.97% patients in CNLA required ICU admission. Though the in hospital mortality rate was 5.55% in CPLA and 1.21% in CNLA. Moortality was observed in these patients due to presentation as a septic shock in these patient on admission due to which multiorgan failure was observed. We did not evaluate any factors associated with mortality in this study. However, the high percentage of invasive procedures performed in 88.9% of patients with liver abscess may be associated with favorable outcomes. According to Sharma MP, Dasarthy S, Verma N et al, mortality rate in their study was 0-18 % as they had performed invasive procedures in 54% of the patients only and treated 46% conservatively. [24].

Recurrence rates were observed by follow up of the patients after 1 month which was observed as 8.3% in CPLA group and 6.09% in CNLA group which was due to incomplete evacuation of the abscess cavity and in patients with liver abscess was caused by drug resistant organisms compared with hyo min yoo et al the recurrence was 9% which was similar to our study.

## 5. Conclusion

Our study suggests that prognosis including presentation as sepsis and recurrence rates were no different in CNLA and CPLA group however Metastatic infections and in hospital mortality were significantly higher and CPLA group compared to CNLA group. Clinical parameters and laboratory parameters were different between both CNLA and CPLA groups and mean hospital stay was higher in CPLA group compared to CNLA group.

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