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A study on bacterial infections and their antibiotic susceptibility pattern in decompensated liver disease patients in a tertiary care Hospital

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Abstract

Background & Objectives: Decompensated liver disease (DCLD) is defined as irreversible chronic injury of the hepatic parenchyma. Bacterial infections are more common in decompensated liver disease and causes 30%-50% of deaths. Therefore, this study was done to determine the various bacterial agents causing infections in decompensated liver disease patients and to determine the drug susceptibility and resistance pattern.

Methods: A prospective study was conducted over a period of one year in a tertiary care hospital. Ascitic fluid, urine, sputum, blood and wound swab were collected. All the samples were processed through Gram's stain and culture. The organisms were identified by standard protocols and antibiotic susceptibility testing.

Results &Conclusion: Out of 150 samples, culture positivity seen in 81(54%). In 81 culture positive isolates, 63(78%) were Gram Negative bacilli (GNB) and 18 (22%) were Gram Positive cocci (GPC). Among Gram negative bacilli, *Escherichia coli* and in Gram positive cocci, *Staphylococcus aureus* was the most common isolates. The most common infections were spontaneous bacterial peritonitis (27%) followed by urinary tract infections (26%), Spontaneous bacteraemia (19%), pneumonia (16%), and skin and soft-tissue infections (12%).

Keywords: Decompensated Liver Disease, Spontaneous Bacterial Peritonitis, *Escherichia coli*, *Staphylococcus aureus*.

Introduction

Liver failure leading to cirrhosis is one of the most common causes of death in our country.[1,2] Cirrhosis is a chronic progressive liver disorder caused by alcoholic liver diseases, viral hepatitis (HBV and HCV) and cryptogenic causes[3] which can leads to liver failure and death.[4] According to the stages of liver injury, signs and symptoms and survival rate, cirrhosis is classified into compensated and decompensated liver disease.[5]

Decompensated liver disease (DCLD) is defined as irreversible chronic injury of the hepatic parenchyma and extensive fibrosis in association with the formation of regenerative nodules and leading to loss of liver function. [6]

Bacterial infections are more common in Patients with decompensated liver disease is due to altered and impaired immunity and causes 30%-50% of deaths.[7] In decompensated liver disease patients, the spontaneous bacterial peritonitis (SBP) is a serious common bacterial infection, followed by urinary tract infections (UTI), spontaneous bacteraemia, pneumonia, and skin infections.[8] The common causative organisms for bacterial infections in DCLD patients are *Enterobacteriaceae*, nonfermentable Gram-negative bacilli and Gram positive cocci and most of them are multidrug resistant.[9,10] The prognosis of these patients is closely related to a prompt and accurate diagnosis and appropriate treatment decreases the mortality rates.

Materials & Methods

A prospective study was conducted over a period of one year. About 150 patients (≥18 yrs.), admitted in various wards with signs & symptoms suggestive of bacterial infections in DCLD patients are included in the study. Ascitic fluid, urine, sputum, blood and wound swab were collected. All the samples were processed through Gram's stain and inoculated onto Blood agar plate, Chocolate agar and MacConkey agar. The inoculated culture plates were incubated overnight at 37°C in an incubator. A Gram's stain was done the next day from the growth and examined. The organisms were identified by standard protocols and antibiotic susceptibility of recommended drugs (CLSI guidelines) was performed by using Kirby Bauer disc diffusion and Minimum inhibitory concentration (MIC) method.

Results

Out of 150 samples, culture positivity seen in 81(54%). In 81 culture positive isolates, 63(78%) were Gram Negative bacilli and 18 (22%) were Gram Positive cocci. Among Gram negative bacilli, *Escherichia coli*was the most common isolates and in Gram positive cocci, *Staphylococcus aureus* was the most common isolates (Table 1). The most common infections were spontaneous bacterial peritonitis (27%) followed by urinary tract infections (26%), Spontaneous bacteraemia (19%), pneumonia (16%), and skin and soft-tissue infections 12%). (Chart 1)

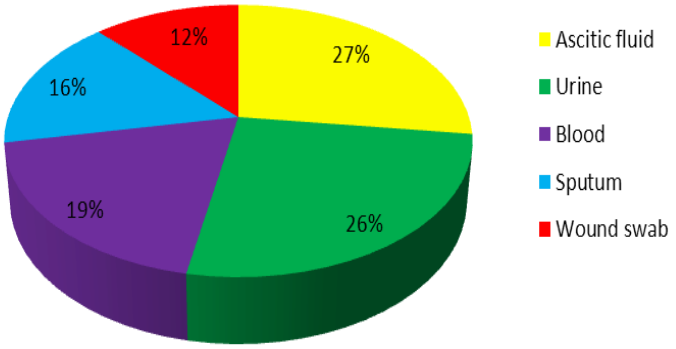

Fig. 1: Distribution of culture positivity in various types of clinical samples in DCLD patients

Table 1: Bacteria isolated from the various samples in DCLD patients

Organisms(no=81)	Ascitic fluid	Urine	Sputum	Skin	Blood	No. of isolates	%of isolates
Escherichia coli	7	8	1	1	2	19	23.5
Klebsiella pneumoniae	3	3	3	1	4	14	17
Klebsiella oxytoca	1	6	6	-	-	13	16
Proteus mirabilis	1	-	-	-	-	1	1.2
Proteus vulgaris	-	-	-	3	-	3	3.7
Enterobacter cloacae	1	1	-	-	-	2	2.5
Citrobacter koseri	1	-	-	-	-	1	1.2
Pseudomonas aeruginosa	1	-	3	1	2	7	9
Acinetobacter baumanii	1	2	-	-	-	3	3.7
Staphylococcus aureus	4	-	-	2	3	9	11
Enterococcus faecalis	2	1	-	-	-	3	3.7
Staphylococcus epidermidis	-	-	-	2	2	4	5
Streptococcus viridians	-	-	-	-	2	2	2.5
Total	22	21	13	10	15	81	100

Most of the organisms were 75% sensitive to amino glycosides and 50% sensitive to fluoroquinolones. All the GNB were 100% sensitive to carbapenem except one carbapenem resistant isolates, *Klebsiella oxytoca* was isolated from sputum sample.

In 81 culture-positive infections, 33(41%) drug resistant bacterial infections were identified: 27 (81%) Extended spectrum Beta Lactamases (ESBL), 4(10%) Methicillin resistant Staphylococcus aureus (MRSA), 1(2.3%) Vancomycin resistant *Enterococci* (VRE) and 1(2.3%) Metallo Beta lactamases (MBL). Of the culture-positive infections, these drug resistant bacterial infections occurred in 11 of 21 (52%) of the UTIs, 8 of 22 (36%) of the SBP, 3 of 15 (20%) of the spontaneous bacteraemia cases, 7 of 13 (54%) of the pneumonia and 4 of 10 (40%) of the skin and soft tissue infection cases.

Fig. 2: Double disk diffusion synergy test for detection of ESBL

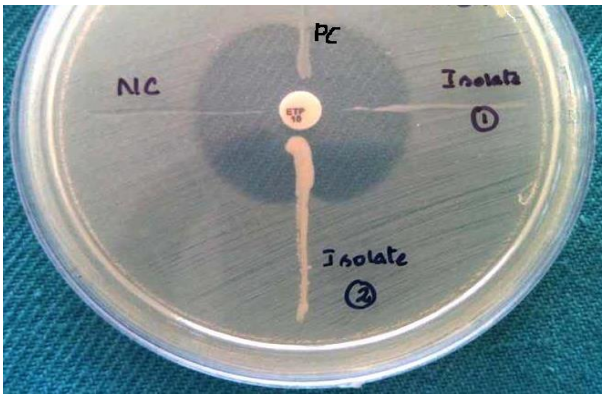

Fig. 3: Modified Hodge Test (MHT)
Isolate 1-Meropenem sensitive –MHT Negative
Isolate 2- Meropenem resistant – MHT Positive

Table 2: Minimum inhibitory concentration (MIC) for detecting drug resistance by macro broth dilution method

Drugs	Organisms	Observed MIC value	Interpretation
Vancomycin	*Staphylococcus aureus(MRSA)* (Isolates no=4)	≤2µg/l	**Sensitive** (≤ 2µg/ml – Susceptible 4-8µg/ml – Intermediate ≥16µg/ml - Resistant.)
Vancomycin	*Enterococcus faecalis*(Isolate no=1)	64µg/ml	**Resistant** (≤ 4µg/ml – Susceptible 8-16µg/ml – Intermediate ≥32µg/ml – Resistant)
Meropenem	*Klebsiellaoxytoca*(Isolate no=1)	≥16µg/ml	**Resistant** (≤ 1µg/ml – Susceptible 2µg/ml – Intermediate ≥4µg/ml – Resistant)

(Interpretation according to CLSI guidelines)

Discussion

In 150 DCLD patients, males 145 (97%) were predominant group when compared to females 5(3%). This predilection of higher frequency rates among male is attributed towards the presence of underlying risk factors like alcoholism.[11,12]

Out of 150 patients of DCLD, 81(54%) were culture positive. In 81 culture positive isolates, 63(78%) were Gram Negative bacilli and 18 (22%) were Gram Positive cocci, which was correlated significantly (P value = 0.005). In decompensated liver disease (DCLD) patients, the most common isolates were Gram negative bacilli which may be due to translocation of normal flora (most of the normal flora in the GIT are GNB) from the gastro intestinal tract. Among bacterial infections, *Escherichia coli* were the most common pathogen (24%).[13]

Among culture positive infections, spontaneous bacterial peritonitis (27%) was the most common infection due to translocation of enteric organisms from the intestine to the peritoneum and diagnostic and therapeutic paracentesis were predisposed to bacterial infections, followed by urinary tract infection (26%), spontaneous bacteraemia (19%), pneumonia (16%) and skin and soft tissues infection (12%).[11,14,15]

In patients with spontaneous bacterial peritonitis (SBP) (27%) the most frequently isolated organisms was *Escherichia coli* (31.82%) as it is the commonest enteric pathogen, followed by *Staphylococcus aureus* (18.18%), *Klebsiella pneumonia* (13.63%) and *Enterococcus faecalis* (9.09%).[19,20]

In this study, among 44 urine samples, 21 (26%) were culture positive. Of which *Escherichia coli* (38.09%) were the most common isolates followed by *Klebsiella oxytoca* (28.57%), *Klebsiella pneumoniae* (14.28%), *Acinetobacter baumanii* (9.52%) and *Enterococcus faecalis* (4.76%). The incidence of urinary tract infection (UTI) is higher in decompensated cirrhotic patients with indwelling urinary catheters.[16]

Among 150 blood samples, 15 (19%) samples were culture positive. Of which *Klebsiella pneumoniae* (26.33%) was the most common isolate followed by *Staphylococcus aureus* (20.00%), *Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus epidermidis* and *Streptococcus viridians.* The Porto systemic shunt

circulation in DCLD patients will favour the organisms to escape from phagocytosis by hepatic reticuloendothelial system, there by establishing systemic bacteraemia.[17]

In the sputum samples, 13(16%) samples were culture positive. *Klebsiella oxytoca* (46.14%) was the most common isolates followed by *Klebsiella pneumoniae* (23.07%) *Pseudomonas aeruginosa* (23.07%) and *Escherichia coli* (7.69%). Some procedures like tracheal intubation, oesophageal tamponade and clinical conditions like hepatic encephalopathy, alcoholism were clearly predisposing factors for pneumonia in cirrhotic patients.

Out of 18 wound swabs, 10(12%) were culture positive. *Proteus vulgaris* (30%) was the main isolate followed by *Staphylococcus aureus* (20%), *Staphylococcus epidermidis* (20%), *Escherichia coli* and *Klebsiella pneumoniae*. Lymphangitis of the lower extremities and abdominal wall are frequent in cirrhotic patients with oedema or ascites which will leads to skin and soft tissue infections in DCLD patients.[17,18]

Most of the organisms were 75% sensitive to amino glycosides and 50% sensitive to fluoroquinolones. All the GNB were 100% sensitive to carbapenem except one carbapenem resistant isolates, *Klebsiella oxytoca* was isolated from sputum sample.

In 81 culture-positive isolates, 31 were drug resistant bacterial infections were identified: 81% (25of 31) were ESBL, 13% (4/31) were Methicillin resistant Staphylococcus aureus, 3% (1/31) were vancomycin resistant Enterococci (VRE), and 3% (1/31) were MBL (3%). Of the culture-positive isolates, these drug resistant bacterial infections occurred in 11 of 21 (52%) of the urinary tract infections (UTIs), 7 of 22 (32%) of the spontaneous bacterial peritonitis (SBP), 3 of 15 (20%) of the spontaneous bacteraemia cases, 6 of 13 (46%) of the pneumonia and 4 of 10 (40%) of the skin and soft tissue infection cases.

Conclusion

The prognosis of DCLD patients is closely related to identify the definitive etiologic diagnosis with its antimicrobial susceptibility and resistant pattern. Antibiotic prophylaxis must be restricted to selected patients and encouraging the use of first line antibiotics and to avoid unnecessary use of higher antibiotics. This will help to lower the occurrence of new resistant strains, which can significantly reduce hospital stay and morbidity and improve survival rate.

References

1. Robbins and Cotran. Pathologic basis of diseases – 8th Edition. Sounder, Elsevier publication.
2. V.A. Sevastianos, S.P. Dourakis. Pathogenesis, diagnosis and therapy of Infections complicating patients with chronic liver disease- Review.
3. Heidelbaugh JJ, Bruderly M. Cirrhosis and chronic liver failure: part I Diagnosis and evaluation. Am Fam Physician. 2006;74:756–762.
4. Salomon JA, Weinstein MC, Hammitt JK, Goldie SJ. Cost-effectiveness of treatment for chronic hepatitis C infection in an evolving patient population. JAMA. 2003;290:228–237.
5. Gennaro D'Amico, Guadalupe Garcia-Tsao, Luigi Pagliaro. Natural history and prognostic indicators of survival in cirrhosis: A systematic review of 118 studies. World J Hepatol. 2006 January;44(1):217-231.
6. Harrison's principle of Internal medicine – 18th Edition.2592-2602.
7. Wong F, Bernardi M, Balk R, Christman B, Moreau R, Garcia-Tsao G, Patch D, Soriano G, Hoefs J, Navasa M. Sepsis in cirrhosis: report on the 7th meeting of the International Ascites Club. Gut. 2005;54:718–725.
8. Papp M, Farkas A, Udvardy M, Tornai. Bacterial infections in liver cirrhosis. Orv 2007 March 4;148(9):387-95.
9. Fernandez J, Gustot T. Management of bacterial infections in cirrhosis. J Hepatol 2012:S1–S12.
10. Arvaniti V, D'Amcio G, Fede G, Manousou P, Tsochatzis E, Pleguezuelo M, *et al.* Infections in patients with cirrhosis increase mortality four-fold and should be used in determining prognosis. Gastroenterology 2010;139:1246-1256.
11. Mathurin S, Chapelet A, Spanevello V, Sayago G, Balparda C, Virga E, Beraudo N, Bartolomeo M. Infections in hospitalized patients with cirrhosis. 2009;69(2):229-38.
12. C Homann, K Varming, K H0gasen, T E Mollnes, N Graudal, A C Thomsen, P Garred Acquired C3 deficiency in patients with alcoholic cirrhosis predisposes to infection and increased mortality. Gut 1997;44:544-549.
13. Borzio M, Salerno F, Piantoni L, Cazzaniga M, Angeli P, Bissoli F, Boccia S, Colloredo-Mels G, Corigliano P, Fornaciari G, Marenco G, Pistarà R, Salvagnini M, Sangiovanni A. Bacterial infection in patients with advanced cirrhosis: a multicentre prospective study. Dig Liver Dis. 2001 Jan-Feb;33(1):41-8.
14. Puneeta Tandon, M.D. Guadalupe Garcia – Tsao. Bacterial infections, sepsis and multi organ failure in cirrhosis. W. R. Caly and E. Strauss, "A prospective study of bacterial infections in patients with cirrhosis," Journal of Hepatology, vol. 18, no.3,pp. 353–358,1993.
15. Anthony P.P. *et al.* World Health Organization. Journal of Clinical Pathology31:395,1978.
16. Maria Pleguezuelo, Jose Manuel Benitez, Juan Jurado, Jose Luis Montero, and Manuel De la Mata. Diagnosis and management of bacterial infections.
17. Rooby Erachamveettil Hamza, Mashhood Padincharepurathu Villyoth, George Peter, Deni Joseph, Chethan Govindaraju, Devang Chandrakanth Tank, Sreejaya Sreesh, Premalatha Narayanan, Kattoor Ramakrishnan Vinayakumar. Risk factors of cellulitis in cirrhosis and antibiotic prophylaxis in preventing recurrence. *Annals of Gastroenterology* (2014)27,1-6.
18. Mohan P1, Ramu B, Bhaskar E, Venkataraman J. Prevalence and risk factors for bacterial skin infection and mortality in cirrhosis. Ann. Hepatology 2011 Jan-Mar;10(1):15-20.
19. Hoefs JC, Canawati HN, Sapico FL, Hopkins RR, Weiner J, Montgomerie JZ. Spontaneous bacterial peritonitis. Hepatology. 2002;2:399–407.
20. Weinstein MP, Iannini PB, Stratton CW, Eickoff TC. Spontaneous bacterial peritonitis: A review of 28 cases with emphasis on improved survival and factors influencing prognosis. *Am J Med*. 2000;64:592–8.