Research Article

A STUDY OF PATTERN OF INFECTIONS IN CHRONIC LIVER DISEASE- A HOSPITAL BASED CROSS SECTIONAL STUDY

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Abstract

Background: Chronic liver diseases (CLDs) are defined as the continuity of clinical and biochemical evidence of hepatic dysfunction for more than six months. Global prevalence of cirrhosis from autopsy studies ranges from 4.5% to 9.5% of the general population. Globally, alcohol consumption, hepatitis B (HBV) and hepatitis C (HCV) has been the main causes of cirrhosis. More recently, increasing incidence of cirrhosis secondary to non-alcoholic fatty liver disease (NAFLD), especially in developed countries. Liver cirrhosis has emerged as a major cause of global health burden. Cirrhosis with ascites has impaired antimicrobial or opsonic activity especially for organism which commonly cause spontaneous bacterial peritonitis. The objective is to study the pattern of various infections in chronic liver disease patients including site of infections, organism associated, and drug sensitivity. **Materials and Methods:** A cross sectional study was conducted from October 2014 to September 2016, in the Department of Medicine, Regional Institute of Medical Sciences (RIMS) Hospital, Imphal, Manipur. All chronic liver disease patients during the study period were included in the study. The study variables for the study are alcoholics, non-alcoholics, hepatitis B infection, hepatitis C infection, autoimmune hepatitis etc. Data collected were analyzed using SPSS-version-21. Either $\chi 2$ test or Fisher's exact test were used for categorical variables, and t-test for continuous variables. A p-value of <0.05 was taken as significant. **Result:** Out of 100 chronic liver disease patients, infections were observed in 47% patients of CLD. The most common infection observed were Urinary tract infection (36%), Spontaneous bacterial peritonitis (10%), Tuberculosis both pulmonary and extrapulmonary (6%), Pneumonia and uncommon infection like Enteric fever and Oropharyngeal candidiasis (5%). Infections were common in patients of CTP -class C (54.23%) and CTP - class B (39.45%) and no infections were reported in patients of CTP-class A. Infections were reported only in decompensated cirrhosis patients (48.45%). 14 patients presented with hepatic encephalopathy and infection were reported in 12 patients. Acute on chronic liver failure (ACLF) was reported in 37% patients. Infections were reported in 20 patients of ACLF. Mortality rate was 5%. **Conclusion:** CLD patients are prone to have sepsis and are more common in CTP C .Sepsis is the major cause of mortality among CLD patients. Early recognition of infections among CLD patients and prompt treatment with appropriate antibiotics will decrease recurrent hospitalization and mortality among CLD patients.

INTRODUCTION

Chronic liver diseases (CLDs) are defined as the continuity of clinical and biochemical evidence of hepatic dysfunction for more than six months.[1] Global prevalence of cirrhosis from autopsy studies ranges from 4.5% to 9.5% of the general population.[2,3] Globally, alcohol consumption, hepatitis B (HBV) and hepatitis C (HCV) has been the main causes of cirrhosis. More recently, increasing incidence of cirrhosis secondary to non-alcoholic fatty liver disease (NAFLD), especially in developed countries.[4] Liver cirrhosis has emerged as a major cause of global health burden. According to

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the WHO, alcohol consumption accounts for 3.8% of the global mortality and 4.6% of DALYs. Liver disease represents 9.5% of alcohol-related DALY's worldwide. In Asian countries like India, alcohol is emerging as the commonest cause of chronic liver disease.[5] Overall rate of HBsAg positivity has been reported to range between 2% and 8% in India.[6-8] Carrier rate in India of 4.7% with an estimated carrier population of 56.5 million. Hepatitis C virus (HCV) is a globally prevalent pathogen and a leading cause of death and morbidity.[9] The most recent estimates of disease burden show an increase in seroprevalence over the last 15 years to 2.8% equating to >185 million infections worldwide.[10] Globally, the prevalence of NASH ranges from 6% to 35% with a median of 20%. Bacterial translocation (BT) is defined by the passage of viable indigenous bacteria from the intestinal lumen to mesenteric lymph nodes (MLNs) and other territories. Cirrhosis with ascites has impaired antimicrobial or opsonic activity especially for E. coli, Streptococcus faecalis and Pneumococci, organism which commonly cause spontaneous bacterial peritonitis. Urinary tract infections (UTI) represent 20%-40% of bacterial infections in prospective studies of hospitalized patients with cirrhosis.[11-15] Overall prevalence of pneumonia in cirrhotics is 15%.[16-19] Other associated infections are tuberculosis, bacterial meningitis, bacterial endocarditis, oral candidiasis Multiresistant bacteria are more frequently isolated in nosocomial infections (35%-39%) compared with HCA (14%-20%) or community-acquired episodes (0%-4%).[20-25] Bacterial infection is responsible for up to a quarter of the deaths of patients with chronic liver disease.[26]Purpose of this study was to find out pattern of different types of infection and their drug sensitivity in patients of chronic liver disease so that early recognition of pathogen and appropriate treatment will decrease mortality.

MATERIALS AND METHODS

This study was a Cross Sectional descriptive studied in the Department of Medicine in collaboration with Department of Pathology and Department of Microbiology, Regional Institute of Medical Sciences (RIMS) Hospital, Imphal, Manipur. A total of 100 patients of age 18 years and above admitted in medicine ward, RIMS Imphal diagnosed with chronic liver diseases (both compensated and decompensated cirrhosis) were included in the study during the period of two years from October 2014 to September 2016. Consent was taken from the patients/ parents/ guardian. A proper history, examination according to written proforma and relevant investigations were carried out. Patients with Diabetes mellitus, end stage renal disease, HIV positive patients presenting with other significant systemic illness and those who refused to participate were excluded from the study. Alcoholics, Non alcoholics, hepatitis B and C infections, Autoimmune hepatitis etc were the study variables.

Working definitions: The diagnosis of Chronic Liver Diseases was made by taking history, clinical examinations, performing mandatory laboratory tests, relevant radio graphical investigations and after ruling out other conditions. Thrombocytopenia is defined as platelet count less than 1.5lakhs/μL.[11] UTI is defined as the presence of more than 10 white blood cells/ml of urine in microscopy in females and more than 5 white blood cells/ml of urine in microscopy in males with symptoms or any urine culture yielding positive results.[12] LRTI is defined as the objective evidence of lung consolidation in radiography in a patient who is symptomatic.[13] SBP is defined as ascitic fluid neutrophil count more than 250cells/μL with or without positive ascitic fluid culture.[14] Survival is defined as patient surviving till the end of the hospital stay or leaving against medical advice prior to the discharge.[15] Mortality is defined as the patient dying due to any cause during the period of hospital stay.[16] Sepsis is defined as life-threatening organ dysfunction caused by an unregulated response of a host. It is manifested by a drop in blood pressure, which decreases tissue perfusion pressure, causing hypoxia that is characteristic of shock.[17]

Data collection: A structured proforma was used. After obtaining informed consent the patients were enrolled in the study. Particulars of patients were taken from record card followed by detailed history and thorough physical examination. Routine investigations were done for all patients and special investigations were done where ever required. The collected data were entered and analyzed in SPSS (IBM) version 21. Summarization of data were carried out by using descriptive statistics such as mean, median, standard deviation and percentages. Either $\chi 2$ test or Fisher's exact test were used for categorical variables, and t-test for continuous variables. P-value < 0.05 was taken as statistically significant. Ethical approval was obtained from the institutional Research Ethics Board before the commencement of the study [Ref.No. AC/112/EC/RIMS/2005].

RESULTS

Infection were observed in 47 patients of CLD. The most common infection were Urinary tract infection (UTI): (36%) followed by Spontaneous bacterial peritonitis (SBP): 10%. Tuberculosis (pulmonary and extrapulmonary): 6%, Pneumonia; 5%, and uncommon infection like Enteric fever and Oropharyngeal candidiasis. In this study infections were reported more in patients of CTP -class C (54.23%) followed by CTP - class B (39.45%) and no infections were reported in patients of CTP-class A. Infection were reported only in decompensated cirrhosis patients (48.45%). Among the study population, 14 patients came with features of hepatic encephalopathy and infection were reported in 12 patients whereas acute on chronic liver failure

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(ACLF) was reported in 37 patients among total study population and out of 37 patients of ACLF, infection were reported in 20 patients. 5% mortality rate were documented among study population and out of 5% infections were reported in 100% and ACLF in 80%.

Average age of the patients was found to be 48.62 years with a standard deviation of 10.80 years. Among study population most of the patients belongs to age group 39-48 years (33%) followed by 49-58 years (31%), 29-38 years (18%), 59-68 years (13%), 69-78 years (3%), and 1% in both age group between 19-28, 79-88 years. There is relatively less number of female patients (6%) as against their counterpart male patients (94%).

Table 1: Distribution of patients on the basis of etiology of CLD.

	Parameters	No of cases	%
Cause of CLD	Alcohol + HBV CLD	9	9.0
	Alcohol + HCV CLD	17	17.0
	Alcoholic CLD	70	70.0
	Autoimmune CLD	1	1.0
	Cryptogenic cirrhosis	1	1.0
	HBV CLD	2	2.0
	Total	100	100.0

χ^2 =75.023, DF=5, P<0.001

The most common cause is Alcoholic related disease (96%). Out of them, 70% were Alcoholic CLD only and 17% were associated with hepatitis C and 9% with hepatitis B. Other 4% of CLD were hepatitis B alone (2%), Autoimmune (1%), and Cryptogenic (1%). The variation of percentages among the six types of causes is found to be a very highly significant (P<0.001). So we were concluded that Alcohol and alcohol with viral hepatitis is commonest cause of CLD and alcohol seems to be most important factor for CLD even if viral hepatitis is seen in 28% of the study population. [Table 1]

Table 2: Distribution of infections among CLD patients

Parameters	Total (N=100)	% of infection
Infection	47	47%
No infection	53	-

χ^2 =0.180, DF=1, P=0.671

Table 3: Distribution of infection among chronic liver disease patient

Parameters	Type	N(%)
UTI	Absent	64 (64%)
	Present	36 (36%)
SBP	Absent	90 (90%)
	Present	10 (10%)
Pneumonia	Absent	95 (95%)
	Present	5 (5%)
Tuberculosis	Absent	94 (94%)
	Present	6 (6%)
Enteric fever	Absent	98 (98%)
	Present	2 (2%)
Candidiasis	Absent	99 (99%)
	Present	1 (1%)

χ^2 =38.174, DF=5, P<0.001

There was 47% infection rate among chronic liver disease patients based on the present sample of 100 such patients. The infection rated is tested by x2 and found to be insignificant statistically despite a visible difference of 6% as evident by P=0.671 which is insignificant even at 5% probability level. [Table 2]

Six types of infections were found and their frequency mentioned here in decreasing order. UTI (36%); SBP (10%); Tuberculosis (6%); Pneumonia (5%); Enteric fever (2%) and Candidiasis (1%). Variation among the six types of infection is highly significnt statistically (P<0.001). [Table 3]

Table 4: Distribution of infection among different types of CLD

Type of infection	CLD patients							% of infection among CLD patients
	Alcohol + HBV CLD	Alcohol + HCV CLD	Alcohol CLD	Autoimmune CLD	Cryptogenic cirrhosis	HBV CLD	Total No. of infection	
UTI	3	9	23	0	0	1	36	36%
SBP	2	0	8	0	0	0	10	10%
CAP	2	0	2	0	0	1	5	5%
TB	3	1	2	0	0	0	6	6%
Enteric fever	1	0	1	0	0	0	2	2%
Candid-iasis	0	1	0	0	0	0	1	1%

[Table 4] Shows distribution of infection among different types of CLD. Out of 36 cases of UTI, 23 were documented in alcoholic CLD only, 9 in alcoholic with hepatitis C, and 3 in Alcoholic with hepatitis B. Only one case of UTI was found in hepatitis B CLD. Out of 10 SBP cases, 2 and 8 cases found in Alcoholic with hepatitis B CLD and Alcoholic CLD respectively. In cases of CAP, 2 cases were found Alcoholic with hepatitis B CLD, 2 in Alcoholic CLD, and only 1 case in hepatitis B CLD. Again for TB, 3, 1 and 2 cases were found in Alcoholic with hepatitis B CLD, Alcoholic with hepatitis C CLD, and Alcoholic CLD respectively. Enteric fever was documented in 1 patient of Alcoholic with hepatitis B CLD and 1 patient of Alcoholic CLD. While one case of Oropharyngeal candidiasis was detected in Alcoholic with hepatitis C CLD.

Table 5: Relation of Infection with Child-Turcette-Pugh score

CTP-score	No. of patients (Total=100)	No. of patients with infection (Total=47)	% of infection
A (5-6)	3	0	0
B (7-9)	38	15	39.47%
C (≥10)	59	32	54.23%

χ^2 =32.696, DF=2, P <0.001

It can be concluded that CTP-class C has definitely more chance of infection than that of CTP-class B as well as of class A. At the same time, 54.23% infection was documented in class C followed by class B

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(39.47%) whereas no infection was found in class A. The difference between 54.23% infection and 39.47% infection is tested and found a very highly significant statisitically (P<0.001). [Table 5]

Table 6: Relation of Infection with Cirrhosis

Stage of cirrhosis	No. of patients	No. of patients with infection	% of infection
Compensated	3	0	0
Decompensated	97	47	48.45%

χ^2 **=56.706, DF=1, P <0.001**

N : number of cases, DF : degree of freedom =test, P = probability of difference due to chance factors.

Out of entire study sample of 100 cases, 97 (97%) of patients were belongs to decompensated cirrosis and remaining 3 (3%) belongs to compensated stages of cirrhosis; and all cases of CLD with infection (47%) were found only in patients of decompensated cirrhosis (97%) with an infection rate of 48.45%. Nevertheless, none are infected among the compensated group. Thus it may be concluded that the decompensated stages of cirrhosis is more prone to infection than that of compensated stages of cirrhosis. This statement is supported by a highly significant x2=56.706 with P<0.001. [Table 6]

DISCUSSION

In Asian countries like India, alcohol is emerging as the commonest cause of chronic liver disease.[4] Alcohol abuse is widely prevalent among the general population of Manipur. According to National Family Health Survey (NFHS) - 4; 2015-2016, alcohol consumption among adults (age 15-49 years) population of Manipur is high, in men 52.5% and in women 6.1%.

In this cross-sectional study 100 chronic liver disease patients were enrolled. Out of 100 patients of chronic liver disease 94 were males and 6 females with mean age of 48.62 years with a standard deviation of 10.80 years. Almost similar age group of CLD patients was seen in other studies like Brij Sharma et al,[30] studied were most of the CLD patients from age group 40 to 59 years and mean age was 51.28 years. Among study population 96 patients had history of significant alcohol intake (for male > 80 gm/day and female > 40 gm/day for >10 years). Out of 96 patients,17 were HBsAg positive and 9 were HCV-Ab positive. Nayak NC et al,[32] studied etiologic categorizations among 372 end-stage CLD patients and they were found hepatitis virus related - 48.6% [hepatitis C virus (HCV) - 31.1% hepatitis B virus (HBV) - 15.9%, HCV and HBV - 1.6%]; alcohol related - 23.1% and NALD related - 16.7% .Ray G reported that CLD due to alcohol showed a significant rising trend with early age (mean 48.4 years) and high percentage of decompensated disease (75%) at presentation and high early mortality (63%). In our study, 3 (3%) patients were included in CTP - class A, 38 (38%) in B and 59 (59%) in C. In a study by Brij Sharma et al,[30] 23.2% patients was in CTP class B and 55.5% in CTP class C that is comparable to our study.

In the present study, Infections were documented in 47 patients (47%) and among them, the most frequent types of infections were: urinary tract infection (UTI) : 36%, spontaneous bacterial peritonitis (SBP) : 10%, pneumonia: 5%, tuberculosis (pulmonary and extrapulmonary): 6%, and other uncommon like enteric fever: (2%), candidiasis : (1%). Among them, the most frequent types of infection were: spontaneous bacterial peritonitis (SBP): 31.07%, urinary tract infection (UTI): 25.24% and pneumonia: 21.37%. Maria Lagadinou and Charalambos AG,[39] noticed more frequent infections were pneumonia (30.6%) and SBP (22.2%) followed by gastrointestinal infections (GI) (13.9%) and UTI (8.3%). M Borzio et al,[18] studied on 361 patients (249 males and 112 females; 66 child-Pugh class B and 295 class C

In our study, out of 36% UTI cases 23% were documented in alcoholic CLD [23 cases of UTI among 70 cases of alcoholic CLD (32.85%)]. 9% in hepatitis C with alcoholic CLD [9 cases of UTI among 17 cases of hepatitis C with alcoholic CLD (52.94%)], 3% in hepatitis B with alcoholic CLD [3 cases of UTI found among 9 cases of hepatitis B with alcoholic CLD (33.33%)]. In the present study all 36% of UTI cases were documented in decompensated cirrhosis.

A multicentre prospective study was conducted by M. Borzio et al,[18] found bacterial infection, regardless of the aetiology, is a severe complication of decompensated cirrhosis and they were found that infection is more frequent in patients with decompensated cirrhosis than in those with compensated cirrhosis. In our study out of 36 UTI patients, 14 patients were culture positive and most common organism were found is E. Coli and 85% were sensitive to Nitrofurantoin, 38% to Amikacin, 31% to Imipenem, 23% to Meropenem and Fluoroquinolones, 15% to 3rd generation Cephalosporins and Gentamycin, and 8% to Piperacillin-tazobactam. -E. Coli (Extended - Spectrum beta lactamase producing E. Coli) was the most frequent multiresistant bacteria isolated in UTI (60%). Use of third-generation cephalosporins and long-term norfloxacin prophylaxis are probably important factor for multiresistant bacterial infection. Combination of a carbapenem plus a glycopeptides were used for UTI with sepsis (to cover ESBL-E and E. faecium), oral nitrofurantoin or fosfomycin were used for uncomplicated UTI and HCA and nosocomial infection were treated according to their local guidelines M Borzio et al,[18] documented enteric flora accounted for 62% of infections, Escherichia Coli being the most frequent pathogen (25%).

In our study 10% SBP documented whereas previous studies like M Borzio et al,[18] documented SBP in (23%) of CLD patients, Wanda Regina Caly et al,[41] reported SBP (31.07%) among 170 cases of cirrhosis, Cally WR and Strauss E,[40] reported SBP (31.07%)

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among 170 cases of cirrhosis, Isabel Cirera et al,[27] observed SBP (25%) in 101 cirrhotic patients. Decreasing incidence of SBP compare to previous studies is probably because of the use of prophylactic antibiotic treatment for SBP.

In our study out of 10 SBP cases, gram negative organism were detected in one patient and gram positive in one but culture was positive only in one patient and E. Coli were detected that was sensitive to Meropenem, Imipenem and Linezolid. Nousbaum JB et al,[33] found Gram-negative bacilli are the major cause of SBP, however there is an increasing trend of Gram-positive cocci related SBP. Overall, 20.8% of isolates were multidrug-resistant (MDR) and 10% extensively drug-resistant (XDR). Health-care-associated (HCA) and/or nosocomial infections were present in 100% of MDR/XDR and in 65.5% of non-DR cases. Meropenem was the empirically prescribed antibiotic in HCA/nosocomial infections showing a drug-resistance rate 30.7% while third generation cephalosporins of 43.5%. Overall 30-days mortality was 37.7% (69.2% for XDR and 34.2% for the rest of the patients, p = 0.015).

In present study all cases of SBP were found in decompensated cirrhosis (CTP - class B: 1 cases, CTP - class C : 9 cases). Isabel Cirera et al,[27] found prevalence of bacterial translocation significantly increased according to the Child-Pugh classification: 3.4% in Child A, 8.1% in Child B and 30.8% in Chilc C patients (x2=6.106, p<0.05)

In present study tuberculosis were reported in 6 (6%) patients of CLD. Among tuberculosis patients pulmonary tuberculosis were reported in 3 patients, pulmonary tuberculosis and tuberculous ascites in 1 patient, tuberculous ascites in 1 patient, and tuberculous ascites with tuberculous pleural effusion in 1 patient. Tuberculous pleural effusion was present only in one patient with lymphocytic count - 5700 and ADA- 122.

Sepsis was documented in 8% of the patients and out of 8%, 50% was associated with ACLF and mortality was observed in 50% of sepsis patients. Hepatic encephalopathy were documented more in SBP (60%) cases followed by UTI (25%), and pneumonia (20%). Out of 14 patients of H.E, 12 were associated with infection (85% H.E associated with infection). Comparison done between 12 cases of H.E out of 47 cases of CLD with infection and 2 cases of HE out of 53 patients of CLD without infection (p=0.002, statistically significant). Mortality among H.E with infection was 33.33% and 80% of total mortality were contributed by infection with H.E.

In present study we concluded that the pattern of infection among our study population is comparable to previous studies. According to our study and previous studies suggested that infection does not depends upon the cause of CLD. But some literature suggested that infection were more in alcoholic CLD. Infections in chronic liver disease depends on severity of liver disease. M. Borzio et al,[18] concluded that bacterial infection, regardless of the aetiology, is a severe complication of decompensated cirrhosis, and although frequently asymptomatic, accounts for both longer hospital stay and increased mortality. In our study 54.23% infection was documented in CTP-class C followed by class B (39.47%) whereas no infection was found in class A and difference between 54.23% infection and 39.47% infection was highly significant statistically (P <0.001). In this study all infection were found in decompensated cirrhosis patients (47 cases of infection out of 97 cases of decompensated cirrhosis, infection rate 48.45%) compare to compensated (no infection among 3 cases of compensated cirrhosis) which was statistically very highly significant (p - value < 0.001)

In present study out of 100 patients, ACLF was documented in 37 cases and 20 out of 37 were associated with infection. So ACLF among the total number of patients with infection is 42.55%. Mortality rate among the CLD without ACLF patients (63 cases) is found to be 1.58% whereas the mortality rate among the ACLF patients (37 cases) is 10.81% (P=0.041, statistically significant). Thus we concluded that the mortality among CLD with ACLF is more than CLD without ACLF. Moreau R et al,[22] reported that major precipitating event for the development of decompensation and ACLF is infection. Alcoholic cirrhosis constitutes 50.70% of all underlying liver diseases of ACLF in the Western countries, whereas hepatitis-related cirrhosis constitutes about - 10.30% of all cases of ACLF. However, in most of the Asian countries, hepatitis B constitutes about 70% and alcohol only about 15% of all the etiologies of ACLF.[36-38] In a prospective study from India, the 30 - and 90 - day mortality was 50% and 63%, respectively, which are similar to those found in Western literature. In our study mortality among ACLF during the period of hospitalization was (4 out of 37) 10.8%. Mortality was compared between CLD with infection (4 out of 47, mortality rate: 8.5%) to CLD without infection (1 out of 53, mortality rate: 1.88%) found statistically significant p=0.045. Therefore, finally we concluded that infection is a major cause of mortality among CLD patients and early recognition of infection and appropriate treatment decreases the chance of mortality among CLD patients.

CONCLUSION

This cross-sectional study showed that most of CLD patients have age more than 40 years (76%) whereas 24% of CLD patients were belongs to age less than 40 years. 59% of CLD patients belong to Child-C followed by Child - B (38%) and Child - A (3%).During the study it was observed that 47% of admitted CLD patients were associated with infections and the most common infection was Urinary tract infection (36%), Spontaneous bacterial peritonitis (10%), Tuberculosis (6%), and Pneumonia (5%).Mortality rate among infection group (47%) was 8.5% and non-infected group (53%) was only

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1.88%. Sepsis was documented in all patients of infection with mortality. Thus, infection with sepsis may be a major cause of mortality among CLD patients. Early recognition of infections among CLD patients and treatment with appropriate antibiotics will decrease recurrent hospitalization and mortality among CLD patients.

REFERENCES

1. Suchy FJ. Chronic viral hepatitis in children. Semin Pediatrgastroenterol Nutr 1996: 2:9-14.
2. Melato M, Sasso F, Zancnati F. Liver cirrhosis and liver cancer. A study of their relationship in 2563 autopsies. Zentralbl Pathol 1993:139(1):25-30
3. Graudal N. Leth P, Marbjerg L. Galloe AM. Characteristics of cirrhosis undiagnosed during life: a comparative analysis of 73 undiagnosed cases and 149 diagnosed cases of cirrhosis, detected in 4929 consecutive autopsies. J Intern Med 191;230(2):165-71.
4. Lim YS, Kim WR. The global impact of hepatic fibrosis and end-stage liver disease. Clin Liver Dis 2008;12(4)733-46.
5. Garg V, Garg H. Khan A, Trehanpati N, Kumar A, Sharma BC, et al. Granulocyte colony-stimulating factor mobilizes CD34+ cells and improves survival of patients with acute-on-chronic liver failure. Gastroenterology 2012;142(3):505-12.
6. Abraham P. Viral hepatitis in India. Clin Lab Med 2012;32(2)159-74
7. Thyagarajan SP, Jayaram S, Mohanavalli B. Prevalence of HBV in general population in India. In: Sarin SK. Singal AK, (Eds). Hepatitis B in India: problems and prevention. New Delhi:CBS;1996.p.5-16
8. Prevention of Hepatitis B in India - An Overview. World health organization South-East Asia Regional Office; New Delhi:2002.
9. Cooks GS, Lemoine M, Thursz M, Gore C, Swan T, Kamarulzaman A, et al. Viral hepatitis and Global Burden of Disease: a need to regroup. J Viral Hepat 2013;20(9):600-1
10. Mohd Hanafiah K, Groeger J, Flaxman AD, Wiersma ST. Global epidemiology of hepatitis C virus infection: new estimates of age-specific antibody to HCV seroprevalence. Hepatology 2013;57(4):1333-42.
11. Jinna S, Khandhar PB. Thrombocytopenia. [Updated 2023 Jul 4]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK542208/
12. Michael L. Wilson, Loretta Gaido, Laboratory Diagnosis of Urinary Tract Infections in Adult Patients, Clinical Infectious Diseases, Volume 38, Issue 8, 15 April 2004, Pages 1150–1158.
13. Mahashur A. Management of lower respiratory tract infection in outpatient settings: Focus on clarithromycin. Lung India. 2018 Mar-Apr;35(2):143-149. PMID: 29487250; PMCID: PMC5846264.
14. Riggio O, Angeloni S. Ascitic fluid analysis for diagnosis and monitoring of spontaneous bacterial peritonitis. World J Gastroenterol. 2009 Aug 21;15(31):3845-50. doi: 10.3748/wjg.15.3845. PMID: 19701963; PMCID: PMC2731245.
15. Garland A, Ramsey CD, Fransoo R, Olafson K, Chateau D, Yogendran M, Kraut A. Rates of readmission and death associated with leaving hospital against medical advice: a population-based study. CMAJ. 2013 Oct 1;185(14):1207-14. Epub 2013 Aug 26. PMID: 23979869; PMCID: PMC3787167.
16. Porcel-Gálvez AM, Barrientos-Trigo S, Gil-García E, Aguilera-Castillo O, Pérez-Fernández AJ, Fernández-García E. Factors Associated with In-Hospital Mortality in Acute Care Hospital Settings: A Prospective Observational Study. Int J Environ Res Public Health. 2020 Oct 29;17(21):7951. PMID: 33138169; PMCID: PMC7663007.
17. Srzić I, Nesek Adam V, Tunjić Pejak D. SEPSIS DEFINITION: WHAT'S NEW IN THE TREATMENT GUIDELINES. Acta Clin Croat. 2022 Jun;61(Suppl 1):67-72. PMID: 36304809; PMCID: PMC9536156.
18. Borzio M, Salemo F, Paintoni L, Cazzaniga M, Angeli P, Bissoli F, et al. Bacterial infection in patients with advanced cirrhosis: a multicentre prospective study. Dig Liver Dis 2001;33(1)41-8.
19. Fasolato S, Angeli P, Dallagnese L, Maresio G, Zola E, Mazza E, et al. Renal failure and bacterial infections in patients with cirrhosis: epidemiology and clinical features. Hepatology 2007;45(1):223-9.
20. Realdi G, Fattovich G, Hadziyannis S, Sehalm SW, Almasio P, Noventa F, et al. Survival and prognostic factors in 366 patients with compensated cirrhosis type B: a multicentre study. J Hepatol 1994;21(4):656-66
21. Liaw YF, Lin DY, Chen TJ, Chu CM. Natural course after the development of cirrhosis in patients with chronic type B hepatitis: A prospective study. Liver 1989;9(4):235-41
22. Moreau R, Jalan R, Gines P, pavesi M, Angeli P, Cordoba J, et al. Acute-on-chronic liver failure is a distinct syndrome that develops in patients with acute docompensation of cirrhosis. Gastroenterology 2013;144(7):1426-37.
23. Bajaj JS, Leary JG, Reddy KR. Wong F, Olson JC, Subramanian RM, et al. Second infection independently increase mortality in hospitalized patients with cirrhosis : North American consortium for the study of end-stage liver disease (NACSELD) experience. hepatology 2012;56(6):2328-35
24. Fermandez J, Gustot T. Management of bacterial infections in cirrhosis. J Hepatol 2012;56(12):1-12.
25. Fernandez J, Acevedo J, Castro M, Garcia O, Rodriguez LC, Roca D, et al. Prevalence and risk factors of infections by multiresistant bacteria in cirrhosis: a prospective study. hepatology 2012;55(5):1551-61.
26. Brann OS. Infectious complications of cirrhosis. Curr Gastroenterol Rep 2001;4(4)289-
27. Cirera I, Bauer TM, Navasa M, Vila J, Grande L, Taura P, et al. prevalence of Bacterial translocation of enteric organisms in patients with cirrhosis. J Hepatol 2001;34(1):32-7.
28. Cheruvattath R, Balan V. Infection in end stage liver diseases. J Clin Gastroenterol 2007;4(4):403-11.
29. Brij Sharma, Sujeet Raina, Rishabh Marwah, Neetu Sharma, Madan Kaushik, SS Kaushal. A follow-up study on adult patients with cirrhosis recruited in an open cohort from the hills of Himachal Pradesh. IJHAS 2016;5(1):24-7.
30. International Insitute for population sciences (IIPS) and Macro International 2008. National Family Health Survey (NFHS-4), India. 2015-16: Manipur. Mumbai : IIPS. http;/www.nfhsindia.org/manipur.
31. Mandayam S, Jamal MM, Morgan TR. Epidemiology of alcoholic liver disease. Semin Liver Dis 2004;24(3):217-32.
32. Nayak NC, Jain D, Vasdev N, Gulwani H, Saigal S, Soin A. Etiologic types of end-stage chronic liver disease in adults: analysis of prevalence and their temporal changes from a study on native liver explants. Eur J Gastroenterol Hepatol 2012;24(10):1199-208.
33. Bellentani S, Saccoccio G, Gosta G, Tiribelli C, Manenti F, Sodde M, et al. Drinking habits as cofactors of risk for alcohol induced liver damage. The Dionysos Study Group. Gut 1997;41(4):845-50.
34. Nousbaum JB. Spontaneous bacterial peritonitis in patients with cirrhosis. La presse Medicale 2015,44(12):1235-42.
35. Alexopoulou A. Extensively drug-resistant bacteria are an independent predictive factor of mortality in 130 patients with spontaneous bacterial peritonitis or spontaneous bacteremia. World J Gastroenterol 2016;22(15):4049-56.
36. Jalan R, Gines P, Olson JC, Mookerjee RP, Moreau R, Garcia-TG, et al. Acute-on-chronic liver failure. J. Hepatol 2012;57(6):1336-48.
37. Sarin SK, Kumar A, Almeida JA, Chawla YK, Fan ST, Garg H, et al. Acute-on-chronic liver failure: consensus recommendations of the Asian pacific Association for the study of the liver (APASL). Hepatol Int 2009;3(1):269-82.
38. Lson JC, Kamath PS. Acute-on-chronic liver failure: concept, natural history, and prognosis. Curr Opin Crit Care 2011;17(2):165-9.
39. Maria Lagadinouand Charalambos A. Bacterial infections in cirrhosis patients : a retrospective epidemiologic study in a Greek University Hospital. Clin Hepatol Rep 2015;2(4):1-8
40. Cally WR, Strauss E. A prospective study of SBP in patients with cirrhosis. J Hepatol 2001;17(3):65-8.
41. Wanda Regina Caly, Edna Strauss. A prospective study of bacterial infections in patients with cirrhosis. J Hepatol 1993;18(3):353-8.

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