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Nutritional Status among Patients with Chronic Hepatitis C in the North-Eastern Part of India: A Cross-Sectional Study from the Tribal Belt of India

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ABSTRACT

Malnutrition is very common in liver disease patients. The nutrition status of chronic hepatitis C infected patients was assessed in those with both compensated and decompensated liver disease. A prospective non-interventional observational study was conducted in a tertiary care hospital among patients attending the liver clinic under medicine Outpatient Department (OPD), with follow-up till six months since recruitment. A total number of 100 recruited eligible patients was divided into two groups of 50 patients each, one comprised of subjects with decompensated liver disease and the other one with compensated liver disease. Out of the 100 participants, 85% were males, with the majority of them being aged between 41 and 50 years, and underweight. At every visit, low mean values in triceps thickness and mid-arm circumference were observed among patients with decompensated liver disease compared to those with compensated liver disease, which had a significant difference statistically. The clinical symptoms and severe malnutrition were found to be higher and significantly statistically associated with the decompensated liver disease patients.

Keywords: chronic hepatitis C infection, nutrition, liver disease, malnutrition.

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BACKGROUND

Hepatitis C virus (HCV), an RNA virus that belongs to the *Flaviviridae* family and genus *Hepacivirus*, was discovered in 1989. Hepatitis C virus infection is one of the most common causes of liver cirrhosis and malnutrition worldwide (1), which has an estimated global prevalence of 58 million, with 1.5 million new infections arising per year (2). In India, about 1% of the population is estimated to have chronic HCV infection, with pockets of areas where the prevalence of hepatitis C has been observed to be relatively higher in Punjab, Haryana, Andhra Pradesh, Puducherry, Arunachal Pradesh, and Mizoram (3).

Hepatitis C virus is spread through contact with blood from an infected person, mostly by sharing needles. The incubation period of HCV is 2-26 weeks, with a mean of 6-12 weeks. HCV RNA testing should be performed to assess viral replication and to confirm the diagnosis of HCV infection. The virus affects the liver. Thirty percent of the infected cases present with short-term illness. But persistent infection and long-term chronic infection (70%) is the hallmark of HCV infection. Cirrhosis may develop over a period of five to 20 years after acute infection in 15% to 30% of patients with persistent infection, who have an annual risk of developing either hepatocellular carcinoma or hepatic decompensation, followed by an increased risk of death (4).

Malnutrition is encountered in 65-90% of patients with advanced liver disease. Liver cirrhosis is an end-stage chronic liver disease, in which hepatocyte impairment reduces the liver function, leading to a variety of nutritional metabolic disorders. Malnutrition has a poor impact on the quality of life and increases the progression of chronic liver disease and mortality among cirrhotic patients (5, 6).

Though very few articles were published so far, our research aimed to identify the malnutrition status among patients with liver disease due to hepatitis C based on its chronicity and variation with disease severity. So, the present study was conducted to assess the nutritional status among chronic HCV patients with compensated and decompensated liver disease who were receiving treatment in the Regional Institute of Medical Sciences (RIMS), Imphal, India. ❑

MATERIALS AND METHODS

Study design and setting

A prospective non-interventional observational study was conducted among patients attending the Department of Medicine and Department of Biochemistry of a tertiary care hospital, Regional Institute of Medical Sciences (RIMS), Imphal, North-Eastern India.

Study population

Patients were recruited from December 2013 to November 2014. Thereafter, selected patients were followed-up for six months. Anti-HCV seropositive patients aged over 18 years were included in the study. Exclusion criteria comprised hepatitis-B seropositive patients, HIV positive ones, and those with type 2 diabetes mellitus, chronic kidney diseases, thyroid disease, and chronic alcohol consumption. By convenience sampling method, 100 eligible participants (N=100) were identified and finally recruited for the present study from the medicine OPD. Out of the 100 participants, 50 subjects had compensated liver disease and the remaining half had suffered from decompensated liver disease following HCV infection.

Chronic hepatitis C is defined as patients who are seropositive for HCV antibody in whom hepatic inflammation occurs and necrosis continues for at least six months. There is no gold standard for the assessment of nutritional status in patients with cirrhosis. It is not practical to attempt detailed nutritional assessment in all patients. We did a staged approach, beginning with a complete history and physical examination and proceeding with more detailed testing.

Data resource and measurement

Details on socio-demographic data, alcohol use, smoking history, 24 dietary re-call, clinical symptoms, anthropometric measurements, biochemical measurements, haemogram, and classified participants using Child-Pugh classification were collected. Under anthropometry, body mass index (BMI), mid-arm circumference (MAC) using a measuring tape (cms), and triceps skin folds (TSF) using a caliper (mms) were measured. The BMI was calculated as *per* the "weight in kg/ height in m^2" formula, after accounting for ascetic fluid retention. The mid-arm circumference was measured at the midpoint between the acromion and olecranon in the non-dominant arm. Skinfold

thickness (SFT) is used commonly to estimate fat reserve. The triceps skinfold thickness was measured by a caliper at the midpoint between the acromion and olecranon. For all measures, a value lower than the fifth percentile was considered as a diagnostic of severe malnutrition. Reference values used for this were established from the general population in 1981 (7). The study investigator (SKS) was trained to measure these parameters in view of minimizing their variability. For biochemical data, plasma protein, serum albumin, and total lymphocyte count were analysed. Patients were followed up every two months until three visits since recruitment. At every visit, all parameters were taken and interpreted thereafter.

Ethical clearance

Ethical clearance was obtained from the Institutional Ethics Committee, RIMS, Imphal, India. Written informed consent was obtained from all subjects, with preserving data privacy and confidentiality (Reference number: IEC/183/2013).

Statistical analysis

Data were entered in MS excel 2013 and analysed using Statistical Package for the Social Sciences (SPSS version 20.0). All continuous variables were expressed as either mean (standard deviation – SD) for parametric data or median (range) for non-parametric data. Chi-square test and t-test were used to appropriately assess the statistical difference between compensated and decompensated HCV liver disease. ❑

RESULTS

A total number of 100 eligible patients were included in the present study and divided into two groups of 50 subjects each. The majority of participants (76%) were aged between 41 and 50 years. Subjects had an overall mean (±SD) age of 45.2 (±7.7) years and a mean (±SD) age of decompensated and compensated liver disease of 47.0 (±6.9) and 43.5 (±8.1), respectively. The mean difference between the two groups was found to be statistically significant (p=0.02). Male subjects were predominant (85%) in the present study. About 30% of all patients were businessmen, followed by farmers (17%), housewives (14%), police officers (13%), and others (26%) (Table 1). All of them had a habit of drinking alcohol, with an average (SD) 24 (±6.2)-year alcohol consumption.

The most common presenting symptom was abdominal pain (46%), followed by altered sensorium (43%), and abdominal distension (42%). Leg swellings (40%), altered behaviour (40%), black stools (38%), and vomiting (38%) were frequently reported by patients with decompensated liver disease. All presenting symptoms were more common among decompensated than compensated liver disease, and findings were statistically significant (p <0.05) (Table 2).

Eighteen participants were lost to follow-up, out of which 11 were found to suffer from decompensated liver diseases.

The mean BMI values of study participants were in the range of underweight and had a decreasing but statistically insignificant trend with each follow-up. The mean triceps thickness was reduced up to six months but the overall mean difference visit-wise was insignificant (p >0.05 by ANOVA). Triceps thickness and MAC were significantly lower among patients with decompensated liver diseases compared to those with compen-

Variable	Decompensated HCV liver disease (n=50) No (%)	Compensated HCV liver disease (n=50) No (%)	Total n=100 No (%)	p-value
Age in years				
≤ 40	3 (6.0)	19 (38.0)	22 (22.0)	**<0.001**
41-50	38 (76.0)	20 (40.0)	58 (58.0)	
51-60	3 (6.0)	11 (22.0)	14 (14.0)	
> 60	6 (12.0)	0 (0.0)	6 (6.0)	
Sex				
Male	46 (92.0)	39 (78.0)	85 (85.0)	**0.050**
Female	4 (8.0)	11 (22.0)	15 (15.0)	

TABLE 1. Distribution of study participants by age and sex (N=100)

TABLE 2. Distribution of participants by clinical features (N=100)

Presenting symptoms	Decompensated HCV liver disease (n=50) No (%)	Compensated HCV liver disease (n=50) No (%)	Total (n=100) No (%)	p-value by Chi^2
Pain abdomen	36 (72.0)	10 (20.0)	46 (46.0)	**<0.001**
Altered sensorium	33 (66.0)	10 (20.0)	43 (43.0)	**<0.001**
Abdominal distension	38 (76.0)	4 (8.0)	42 (42.0)	**<0.001**
Swelling legs	20 (40.0)	5 (10.0)	25 (25.0)	**0.001**
Altered behaviour	20 (40.0)	5 (10.0)	25 (25.0)	**0.001**
Black stools	19 (38.0)	2 (4.0)	21 (21.0)	**<0.001**
Fever	16 (32.0)	3 (6.0)	19 (19.0)	**0.001**

TABLE 3. Association between selected variables among patients with decompensated and compensated HCV liver disease

Variables	Decompensated HCV liver disease (mean±SD)	Compensated HCV liver disease (mean±SD)	Total mean±SD	p value by t-test
BMI				
At day 0	16.6 ± 8.6	15.3 ± 10.0	16.01 ± 9.3	0.499
After two months	16.0 ± 7.4	15.1 ± 8.9	15.78 ± 8.3	0.690
After four months	15.8 ± 7.0	15.0 ± 7.2	15.52 ± 8.4	0.570
After six months	14.8 ± 7.1	15.0 ± 7.0	15.43 ± 7.9	0.833
Triceps thickness (mm)				
At day 0	7 .6 ± 3.01	11.9 ± 6.11	9.7 ± 9.3	**<0.001**
After two months	7.4 ± 3.0	10.0 ± 5.2	8.2 ± 8.4	**0.002**
After four months	7.2 ± 3.2	9.9 ± 5.3	8.1 ± 7.5	**0.002**
After six months	6.9 ± 7.1	9.6 ± 7.0	7.9 ± 7.3	**0.050**
Mid-arm circumference (cm)				
At day 0	22.3 ± 2.6	24.3 ± 4.1	23.4 ± 3.6	**0.008**
After two months	22.0 ± 1.9	23.7 ± 3.9	22.5 ± 3.4	**0.003**
After four months	20.7 ± 2.0	23.1 ± 4.0	21.9 ± 3.5	**0.001**
After six months	18.8 ± 2.5	22.7 ± 4.1	20.7 ± 3.9	**0.050**
Serum albumin (g/dL)				
At day 0	2.9 ± 0.3	3.1 ± 0.2	3.3 ± 0.3	**0.002**
After 2 months	2.7 ± 0.2	3.0 ± 0.4	2.9 ± 0.5	**0.003**
After 4 months	2.4 ± 0.3	3.1 ± 0.5	2.8 ± 0.5	**<0.001**
After 6 months	2.1 ± 0.4	2.9 ± 0.5	2.7 ± 0.6	**0.001**

sated liver disease at every visit and were found to be statistically significant. The overall difference in the reduction of mean MAC visit-wise was statistically significant ($p<0.05$ by ANOVA) (Table 3). The average (SD) total lymphocyte count was 1646.3 (468), which was within the normal range.

Out of all participants, 53% had low baseline levels of serum albumin, with lower levels was among those with Child-Pugh Grade C (82%) than

TABLE 4. Association between Child-Pugh classification and serum albumin level at baseline visit (N=100)

Child-Pugh classification	Serum albumin		Total	p value
	Normal No (%)	Low No (%)	No (%)	by Chi²
Grade A	19 (73.0)	7 (27.0)	26 (100)	<0.001
Grade B	21 (60.0)	14 (40.0)	35 (100)	
Grade C	7 (17.9)	32 (82.1)	39(100)	
Total	**47 (47.0)**	**53 (53.0)**	**100 (100.0)**	

other grades. This parameter was found to be statistically significant ($p < 0.001$) (Table 4). ❑

DISCUSSION

The present study assessed the nutritional status of 100 patients with chronic hepatitis C. There was an equal proportion of patients with compensated (50) and decompensated liver disease (50), since the nutritional status can influence disease progression, improve the quality of life, and contribute to the response to treatment. All of them had an appropriate management and were followed-up every two months until six months. Participants to our study had an overall mean (±SD) age of 45.2 (±7.7) years, which was similar to the mean age reported by the study conducted by Silva SE *et al* (8) on 70 chronic hepatitis C patients in Brazil. Since the majority of participants to our study (85%) were males, we assumed that transmission of hepatitis C might have occurred rather via intravenous drug use than sexually. The proportion of decompensated liver disease was high among patients aged over 40 years and had more presenting symptoms. Similarly, Mahajan R *et al* and Sood A *et al* reported that the majority of their patients from Punjab were men and middle aged (9, 10). In the present study, abdominal pain was the most common (46%) complaint, followed by altered sensorium (43%) and abdominal distension (42%), all these complaints being more common in patients with decompensated liver disease than those with compensated disease. Tai MS *et al* (11) reported that most of the hepatitis C patients had abdominal distention (42%), followed by infection (19%), and only few subjects (5%) had pain in the abdomen. This difference between findings might be due to differences in patients' clinical stages.

The relationship between malnutrition and liver disease has been assuming greater significance due to the recognition that it was associated with adverse clinical outcomes. Malnutrition is present in 65-90% of patients with advanced liver disease and almost 100% of candidates for liver transplantation. In the present study, all participants had a low BMI and were therefore considered underweight persons. Malnourished cirrhotic patients have not only a higher morbidity but also an increased mortality rate. As the disease progressed, patients had severe malnourishment, and this pattern would be noted early in the decompensated Child-Pugh C group. The severity of malnutrition has a direct correlation with liver disease progression (5, 6). According to studies across different parts of the world, a wide variation in the percentage of malnutrition, between 12% and 98%, was found among hepatitis C patients, which may be due to differences between methods used for the assessment of nutritional status, including triceps skinfold thickness (TSF), arm muscle circumference (AMC), subjective global assessment (SGA), nutritional risk index (NRI), BMI, Maastricht index (MI), and instant nutritional assessment (INA) (11, 12-15) As a general rule, patients with compensated cirrhosis are more likely to have laboratory investigations which are similar to those of a clinically healthy population compared to those with decompensated cirrhosis. Thus, there is a need for a more detailed assessment among decompensated liver disease patients. However, many standard nutritional assessment tools have limitations when applied to patients with decompensated cirrhosis due to the presence of salt and water retention and advanced hepatic synthetic dysfunction.

In this study, nearly half of patients (53%) had a low baseline level of serum albumin, with the majority of those with Child-Pugh Grade C (82%) having low serum albumin levels. With the increased disease severity, the serum albumin level was reduced and found to be statistically significant ($p < 0.001$). Similar findings were reported in studies done by Ismail FW *et al* (12) Tai MS *et al* (11), Lautz HU *et al* (14), Yasutake K *et al* (16), Roongpisuthipong *et al* (17), and Somi MH *et al* (18). Thus, high protein intake for patients with hepatitis C liver disease should be advised if diagnosed with protein and albumin deficiency in their serum, followed by regular assessment of serum albumin levels. Strengths of the present study comprise the inclusion of compensated and decompensated hepatitis C liver disease patients

and use of three different methods of nutrition assessment to avoid measurement bias.

Study limitations

Our study has some inherent limitations, including the small sample size and geographically limited catchment area of participants. In the future, other diagnostic work-up such as fasting lipid profile and diabetic status need to be considered to comment on overall metabolic findings in chronic hepatitis C patients. The findings of the present study could not be generalised since it was restricted to patients who visited a hospital setting. ❑

CONCLUSIONS

In conclusion, we found that underweight was prevalent among all participants in our study who had a diagnosed HCV infection, with progressive severity and intensity throughout the entire spectrum of HCV disease. Patients with decompensated liver disease and having poor Child-Pugh classification (grade C) were significantly malnourished. Thus, regular assessment of nutritional status and maintaining adequate protein intake for hepatitis C liver disease patients are recommended. A large multicentric longitudinal study is needed to explore the exact causality among patients with chronic hepatitis E virus infection.. ❑

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Authors' contributions: SKS conceptualized the research and collected the data. BDS and MS were involved in data analysis and interpretation. The manuscript was drafted by MS. The draft was reviewed by GKD and PNK, who provided expert opinions. All authors gave the final approval of the manuscript to be submitted for publication.

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References

1. **Sharma N, Singh MM, Ingle GK, Jiloha RC.** An epidemiological study of cigarette smoking among male college students of Delhi University. *Indian J Community Med* (Internet) 2006 Jan (cited 2020 Apr 12); 31(1):35. Available from: http://www.ijcm.org.in/temp/IndianJCommunityMed31135-4472079_122520.pdf
2. **World Health Organization.** Interim guidance for country validation of viral hepatitis elimination (Internet). Geneva: World Health Organization, 2021 (cited 2022 Jan 1). Available from: https://apps.who.int/iris/handle/10665/341652
3. **Ministry of Health & Family Welfare.** Government of India. Viral Hepatitis - The Silent disease facts and treatment guidelines. National Centre for Disease Control. https://ncdc.gov.in/linkimages/guideline_hep20158117187417.pdf
4. **Butt AA.** Hepatitis C virus infection: the new global epidemic. *Expert Rev Anti Infect Ther* 2005;3:241-249.
5. **Silva LD, Bering T, Rocha GA.** The impact of nutrition on quality of life of patients with hepatitis C. *Curr Opin Clin Nutr Metab Care* 2017;20:420-425.
6. **Ismail FW, Khan RA, Kamani L, et al.** Nutritional status in patients with hepatitis C. *J Coll Physicians Surg--Pak JCPSP* 2012;22:139-142.
7. **Rona RJ, Chinn S.** The National Study of Health and Growth: nutritional surveillance of primary school children from 1972 to 1981 with special reference to unemployment and social class. *Ann Hum Biol* 1984;11:17-27.
8. **Silva VA de SE, Ferraz MLG, Carvalho-Filho R de, et al.** Association of the nutritional profile with histological findings of patients with genotype 1 chronic hepatitis C infection. *Arq Gastroenterol* (Internet) 2015 Dec (cited 2022 Jan 2);52:315–20. Available from: http://www.scielo.br/j/ag/a/FZpHsvThMGSWs86jR9mSzzv/?lang=en.
9. **Mahajan R, Midha V, Goyal O, et al.** Clinical profile of hepatitis C virus infection in a developing country: India. *J Gastroenterol Hepatol* 2018;33:926-933.
10. **Sood A, Suryaprasad A, Trickey A, et al.** The burden of hepatitis C virus infection in Punjab, India: A population-based serosurvey. *PloS One* 2018;13:e0200461.
11. **Tai M-LS, Goh K-L, Mohd-Taib SH, et al.** Anthropometric, biochemical and clinical assessment of malnutrition in Malaysian patients with advanced cirrhosis. *Nutr J* (Internet) 2010 Jun 24 (cited 2022 Jan 6);9:27. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2909148/.
12. **Ismail FW, Khan RA, Kamani L, Wadalawala AA, Shah HA.** *Nutritional status in patients with hepatitis C.* 2012;22:6.
13. **Kawabe N, Hashimoto S, Harata M, et al.** Assessment of nutritional status of patients with hepatitis C virus-related liver cirrhosis. *Hepatol Res* (Internet) 2008 (cited 2022 Jan 6);38(5):484–90. Available from: https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1872-034X.2007.00300.x.
14. **Lautz HU, Selberg O, Körber J, et al.** Protein-calorie malnutrition in liver cirrhosis. *Clin Investig* (Internet) 1992 Jun 1 (cited 2022 Jan 6);70(6):478–86. Available from: https://doi.org/10.1007/BF00210228.
15. **Luong R, Kim M, Lee A, Carey S.** Assessing nutritional status in a cohort of liver cirrhosis outpatients: A prospective cross-sectional study. *Nutr Health* 2020;26:19-25.
16. **Yasutake K, Bekki M, Ichinose M, et al.** Assessing current nutritional status of patients with HCV-related liver cirrhosis in the compensated stage. *Asia Pac J Clin Nutr* 2012;21:400-405.
17. **Roongpisuthipong C, Sobhonslidsuk A, Nantiruj K, Songchitsomboon S.** Nutritional assessment in various stages of liver cirrhosis. *Nutr Burbank Los Angel Cty Calif* 2001;17:761-765.
18. **Somi M, Rahimi A, Moshrefi B, et al.** Nutritional Status and Blood Trace Elements in Cirrhotic Patients. *Hepat Mon* (Internet) 2007 (cited 2022 Jan 6);7(1):27-32).