International Journal of Advanced Multidisciplinary Research
ISSN: 2393-8870
www.ijarm.com
DOI: 10.22192/ijamr Volume 4, Issue 8 -2017

Research Article

DOI: http://dx.doi.org/10.22192/ijamr.2017.04.08.005

# To study and evaluate the prevalence and pattern of peripheral neuropathy in patients of cirrhosis of liver in rural population of Uttar Pradesh

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**Keywords**

Cirrhosis of liver, peripheral neuropathy, sensorymotor, liver biopsy.

## Abstract

**Background**: Cirrhosis of liver is an emerging and one of the major global health problem and it is an important cause of morbidity and mortality globally. It is also one of the most common cause of death worldwide. There are different mechanisms of liver injury that lead to inflammation and fibrogenesis and results into cirrhosis. Histologically it is characterized by diffuse nodular regeneration surrounded by dense fibrotic septa with subsequent parenchymal extinction and collapse of liver structures, together causing pronounced distortion of hepatic vascular architecture.

**Material and Methods:** The study was conducted in the Department of Medicine, Government Medical College, Kannauj during 2015-2016. Patient was diagnosed to be having cirrhosis of liver by presence of symptoms and signs of chronic liver cell dysfunction in association with evidence of portal hypertension (portal vein diameter> 12mm and presence of oesophageal varices) with or without .liver biopsy shall be the subjects of present study.

**Results**: We observed that in 75 patients of peripheral neuropathy, 39(52%) patients had polyneuropathy and 36 (48%) patients had mononeuropathy multiplex and among 39 patients of polyneuropathy, 28 (71.8%) patients had sensory motor demyelinating type and 11 (28.2%) patients had sensorymotor axonal type of polyneuropathy

**Conclusion:** Peripheral neuropathy was seen in 75% of patients of cirrhosis of liver. Polyneuropathy was seen in 52% of cirrhotic patients while mononeuropathy multiplex was seen in 48% of cirrhotic patients. Sensory motor demyelinating type of polyneuropathy was seen in 71.8% and sensorymotor axonal type of polyneuropathy was seen in 28.2% patients of cirrhosis of liver.

## Introduction

Cirrhosis of liver is an emerging and one of the major global health problem and it is an important cause of morbidity and mortality globally. It is also one of the most common cause of death worldwide. There are different mechanisms of liver injury that lead to necro inflammation and fibrogenesis and results into cirrhosis. Histologically it is characterized by diffuse nodular regeneration surrounded by dense fibrotic septa with subsequent parenchymal extinction and collapse of liver structures, together causing pronounced distortion of hepatic vascular architecture[1, 2].

Since the liver plays an important role in the storage and transport of cobalamin, it is not surprising that liver pathology is associated with major changes in plasma cobalamin concentrations. For example in acute hepatitis, elevated levels in plasma have been found in 25 to 40% of the patients[3,4].

Inflammation-induced cell degradation thereby causes the release of stored cobalamin, which in the circulation predominantly binds to HC (Haptocorrin). This latter process becomes reinforced by a diminished concentration of TC II (Transcobalamin II), which is the result of an impaired synthesizing capacity of the liver. In liver cirrhosis the increase of plasma cobalamin is also associated with tissue depletion. Several studies show a significant decrease of intracellular cobalamin in liver biopsies.[5-7]

Peripheral neuropathy need to be focused as it is important complication of cirrhosis of liver that may seriously impair patient's routine daily activities and quality of life. Various studies revealed prevalence of peripheral neuropathy varying from 19-80% in the cirrhotic patients on nerve conduction studies.[7-14]

Peripheral nerve dysfunction is significantly more frequent in advanced liver disease compared with early liver damage.Some diseases producing liver dysfunction can independently cause peripheral neuropathy. Hence, a cause and effect relationship between liver disease and neuropathy has been questioned. Alcohol consumption is one such hypothesis. Autonomic neuropathy has also been reported in association with chronic liver disease.[15–22]

## Materials and Methods

### Place of Study

The study was conducted in the Department of Medicine government medical college,kannauj during 2015-2016.

### Inclusion Criteria:

All those patients admitted in Department of Medicine, Government Medical College, Kannauj shall be the subjects of present study.

Patient was diagnosed to be having cirrhosis of liver by presence of symptoms and signs of chronic liver cell dysfunction in association with evidence of portal hypertension (portal vein diameter> 12mm and presence of oesophageal varices) with or without liver biopsy shall be the subjects of present study.

### Exclusion Criteria:

- Overt Hepatic Encephalopathy
- Diabetic neuropathy
- Cerebrovascular disease
- Primary neurological disorder
- Chronic renal failure
- Surgical gastrectomy
- Malabsorption syndrome
- Human immunodeficiency virus disease

Based on inclusion and exclusion criteria a total of 100 patients were selected.Patient those enrolled in study were evaluated for:

- Patients personal detail- Name, Age, Sex, Socioeconomic status according to Kuppuswamy classification, Address
- Presenting complaint- Fever, nausea, vomiting, yellowish discoloration of eyes and urine, pain abdomen, distension of abdomen, hematemesis, malena.following investigations were performed Hemoglobin
  - Total leucocytes count
  - Differential count
  - General blood picture
  - Platelet count
  - Random blood sugar
  - Serum Na+, Serum K+
  - Serum Urea, Serum Creatinine
  - Prothrombin time, International normalized ratio

### Liver Function Test:

- Serum Bilirubin (total and direct)
- Serum glutamic-pyruvic transaminase (SGPT)
- Serum glutamic oxaloacetic transaminase (SGOT)
- Serum Alkaline Phosphatase
- Serum Total Protein
- Serum Albumin

### Ultrasound Abdomen:

- Liver echo texture
- Portal Vein Diameter
- Size of liver & spleen
- Ascites

### Upper Oesophago Gastro Duodenoscopy:

- For assessing varices

### Ascitic Fluid Analysis:

- Total leucocytes count
- Differential count
- Ascitic/ Serum protein
- Ascitic/Serum albumin
- AFB and Gram stain

### Serum Vitamin B12

### Serum Homocysteine

### Nerve conduction velocity test

### Statistical analysis

After completion of data, the statistical analysis has been done with help of unpaired t test, Chi Square test; Spearman Correlation coefficient test and conclusion were drawn. The p-value<0.05 was considered significant. All the analysis was carried out by using SPSS 16.0 version.

## Results

**Types of polyneuropathy in patients of liver cirrhosis**

| Polyneuropathy | No. of patients (n=39) | Percentage |
|---|---|---|
| Sensory motor demyelinating polyneuropathy | 28 | 71.8 |
| Sensory motor axonal polyneuropathy | 11 | 28.2 |

**Distribution of peripheral neuropathy in different etiology of liver cirrhosis**

| Cirrhosis of liver | Total no. of patients (N=75) | Type of neuropathy | | | | p-value |
|---|---|---|---|---|---|---|
| | | Polyneuropathy | | Mononeuropathy Multiplex | | |
| | | No. | % | No. | % | |
| **Alcoholic** | | | | | | |
| Yes | 26 | 12 | 46.2 | 14 | 53.8 | 0.46 |
| No | 49 | 27 | 55.1 | 22 | 44.9 | |
| **HBsAg** | | | | | | |
| Positive | 23 | 12 | 52.2 | 11 | 47.8 | 0.98 |
| Negative | 52 | 27 | 51.9 | 25 | 48.1 | |
| **HCV** | | | | | | |
| Positive | 26 | 15 | 57.6 | 11 | 42.3 | 0.32 |
| Negative | 49 | 23 | 46.9 | 25 | 51.1 | |

**Distribution of peripheral neuropathy according to Child Pugh classification in patients of liver cirrhosis**

| Child Pugh class | No. of patients (n=100) | Peripheral Neuropathy | | | | p-value |
|---|---|---|---|---|---|---|
| | | Present | | Absent | | |
| | | No. | % | No. | % | |
| A | 32 | 20 | 62.5 | 12 | 37.5 | 0.02* |
| B | 40 | 30 | 75.0 | 10 | 25.0 | |
| C | 28 | 25 | 89.2 | 3 | 10.7 | |

**Distribution of Serum Vitamin B12 in patients of liver cirrhosis with and without peripheral neuropathy**

| Patients of cirrhosis of liver | Serum Vitamin B12 (pg/ml) (Mean±SD) |
|---|---|
| With peripheral neuropathy | 1953.73±301.40 |
| Without peripheral neuropathy | 887.48±492.67 |
| p-value | 0.0001* |

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## Discussion

Peripheral neuropathy is a common complication of liver cirrhosis but seldom discussed because most of the patients remain asymptomatic but it gradually distorts the peripheral nervous and causes significant morbidity. Hence early screening of peripheral neuropathy in patients of liver cirrhosis should be done to prevent gross damage to peripheral nervous system which hampers daily routine activities of a patient. Vitamin B12 deficiency is one of the most common causes of nutritional anemia's but it may also affect the peripheral nervous system. Hence our study was conducted to evaluate the prevalence and pattern of peripheral neuropathy in patients of cirrhosis of liver and its association with serum vitamin B12 levels.

In our study we observed that in 75 patients of peripheral neuropathy, 39(52%) patients had polyneuropathy and 36 (48%) patients had mononeuropathy multiplex and among 39 patients of polyneuropathy, 28 (71.8%) patients had sensorymotor demyelinating type and 11 (28.2%) patients had sensorymotor axonal type of polyneuropathy and similar study done by **Dayan *et al.***[78] and **Chari V R *et al.***[13] in which they concluded that patients of liver cirrhosis with different etiology has demyelinating type of polyneuropathy.

Different etiologies of liver cirrhosis were evaluated in which 39 patients were alcoholic liver cirrhosis, 31 patients were HBsAg related cirrhosis and 30 patients were HCV related cirrhosis and we found that 26 (67%) patients of alcoholic liver cirrhosis had peripheral neuropathy whereas 23 (74%) patients and 26 (86%) patients of HBsAg and HCV related cirrhosis had peripheral neuropathy respectively thus different etiological classes of liver cirrhosis had no significant association with peripheral neuropathy and we also found that patients of liver cirrhosis due to alcoholism had no significant difference with peripheral neuropathy caused by non alcoholic liver cirrhotic patients and this finding supported by a study done by **Kharbanda *et al.***[12] in which they concluded that regardless of the etiology of cirrhosis, the cause of neuropathy was probably the liver disease itself, as the incidence and severity of neuropathy in the alcohol-related cirrhosis, although higher.

To evaluate the association of peripheral neuropathy with the severity of liver cirrhosis, we classified patients of liver cirrhosis on the basis of Child Pugh Severity score in which 32 patients belongs to class A, 40 patients in class B and 28 patients in class C and we observed that 20 patients (62.5%) had peripheral neuropathy in class A patients whereas 30 patients (75%) and 25 patients (89.2%) had peripheral neuropathy in class B and class C respectively and we found statistically significant association of peripheral neuropathy with the severity of liver disease and in favor of our study done by Fawi GH *et al.*

In our study Serum Vitamin B12 levels were assessed and the higher levels of Serum Vitamin B12 with a mean value of 1698.22±553.10 (pg/ml) found in an age group of 50-60 years and high levels of Serum Vitamin B12 was found in female patients of liver cirrhosis with a mean value of 1757.70±529.22 (pg/ml) and Serum Vitamin B12levels assessed in different etiology of liver cirrhosis with peripheral neuropathy however statistically no significant association has been found and we also stratified the Serum Vitamin B12 levels according to Child Pugh classification and we observed that high levels of Serum Vitamin B12 with mean value of 1693.21±543.12 (pg/ml) were seen in Child Pugh Class C patients of liver cirrhosis but the levels of Serum Vitamin B12 have no significant association with severity of liver disease. (p=0.78)

## Conclusion

We conducted a study in which we observed pattern of peripheral neuropathy in patients with different etiological classes of liver cirrhosis and its association with serum vitamin B12 levels.

The following conclusions were drawn from our study:

1. We enrolled 100 patients of cirrhosis of liver and mean age of the study group was 49.78±11.33 years.
2. Peripheral neuropathy was seen in 75% of patients of cirrhosis of liver.
3. Polyneuropathy was seen in 52% of cirrhotic patients whilemononeuropathy multiplex was seen in 48% of cirrhotic patients.
4. Sensorymotor demyelinating type of polyneuropathy was seen in 71.8% and sensorymotor axonal type of polyneuropathy was seen in 28.2% patients of cirrhosis of liver.
5. Peripheral neuropathy was seen in 62.5% of Child Pugh Class A, and 75% of Child Pugh Class B and 89.2% of Child Pugh Class C patients of liver cirrhosis and was statistically significant and thus peripheral neuropathy associated with severity of liver dysfunction.
6. The mean Serum Vitamin B12 levels in patients of cirrhosis of liver with peripheral neuropathy were compared with patients of cirrhosis of liver without peripheral neuropathy and we found that Serum Vitamin B12 levels were statistically significantly raised.

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| DOI:10.22192/ijamr.2017.04.08.005 | |

How to cite this article:
Mohammad Amzarul, Sara Siddiqui. (2017). To study and evaluate the prevalence and pattern of peripheral neuropathy in patients of cirrhosis of liver in rural population of Uttar Pradesh. Int. J. Adv. Multidiscip. Res. 4(8): 28-33.
DOI: http://dx.doi.org/10.22192/ijamr.2017.04.08.005