

## Original Research

### A study of autonomic dysfunction in liver cirrhosis

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#### ABSTRACT:

**Background:** To study autonomic dysfunction in liver cirrhosis. **Materials & methods:** Patients with liver cirrhosis admitted in medicine ward from JAN 2019 to JUN 2020 were included in the study. The age group included was > 18 years. The association between two qualitative variables chi-square and Yate's correction test applied at 95% level of significance. Thus p value less than 0.05 was considered as statistically significant. Comparison of the mean of more than two independent quantitative variables ANOVA was applied at 95% level of significance. **Results:** 8 patients were diagnosed with LC within a year, out of which 5 patients were without AD and 3 patients had early AD. Total 16 patients were diagnosed with LC for more than 1 year but less than 3 years. Among them 2 patients were without AD, 13 patients had early AD and 1 patient had definite AD. 8 patients had duration of liver cirrhosis between 4 to 6 years and in this group 1 patient was without AD, 4 had early AD and other 3 had definite AD. **Conclusion:** Severity of autonomic dysfunction increase with duration of liver cirrhosis.

**Keywords:** liver cirrhosis, dysfunction, severity.

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#### INTRODUCTION

Cirrhosis of liver is a global health problem and leading cause of morbidity and mortality. With the ever-expanding population, improvements in treatment, and the subsequent improvement in survival, the Liver cirrhosis (LC) population is expanding. While advancing prognosis may be considered beneficial for patients a longer life does not always equate to an improved quality of life.<sup>1,2</sup> One of the major contributors to a poor quality of life in LC is autonomic dysfunction (AD)<sup>3,4,5</sup> and while the evidence base for the treatment of LC continues to expand, the evidence for symptom control and palliation is being left behind.

The pathogenesis of autonomic neuropathy in cirrhosis of liver is not fully understood. Several mechanisms have been suggested like circulatory changes in cirrhosis, metabolic and neurohormonal alteration. The sympathetic (SNS) and parasympathetic nervous systems (PNS) form the two arms of the ANS through which viscera, smooth muscle and secretory glands are controlled involuntarily. The physiological responses of

sympathetic nervous stimulation on cardiovascular system are increased heart rate (HR) and blood pressure (BP). The neurotransmitter of the parasympathetic nervous system is acetylcholine. The stimulation of the parasympathetic nervous system causes the cardiovascular clinical responses like decreased HR and contractility. Liver disease results in a decreased response to vasoconstrictors which may be caused by increased concentration of vasodilators such as nitric oxide. An increase in portal blood pressure, even mild, can lead to an up-regulation of nitric oxide synthetase.<sup>6</sup> An increase in circulating vasodilators due to increased concentration of nitric oxide, a diseased liver and a portosystemic circulation bypassing hepatic metabolism will contribute to increased systemic vasodilatation. Circulating vasodilators will activate the renin-angiotensin-aldosterone system (RAAS) and increase plasma levels of the vasoconstrictor angiotensin II. Angiotensin II may interact with the parasympathetic control of heart rate variability (HRV). Infusion of angiotensin II causes a decrease in HRV and a reduction in vagal discharges to the heart. Hence, this

study was conducted to study autonomic dysfunction in liver cirrhosis.

## MATERIALS & METHODS

Patients with liver cirrhosis admitted in medicine ward from JAN 2019 to JUN 2020 were included in the study. The age group included was > 18 years. The diagnosis of cirrhosis was based on history, clinical features and ultrasonography. Patients were subjected to symptom analysis, clinical examination and laboratory investigations. A structured clinical proforma was used for data collection in which all pertinent details of the patients were recorded. Apart from routine clinical examination and investigations, standard autonomic testing was done in all the patients to detect autonomic dysfunction. The association between two qualitative variables chi-square and Yate's correction test applied at 95% level of significance. Thus p value less than 0.05 was considered as statistically significant. Comparison of the mean of more than two independent quantitative variables ANOVA was applied at 95% level of significance.

## RESULTS

8 patients were diagnosed with LC within a year, out of which 5 patients were without AD and 3 patients had early AD. Total 16 patients were diagnosed with LC for more than 1 year but less than 3 years. Among them 2 patients were without AD, 13 patients had early AD and 1 patient had definite AD. 8 patients had duration of liver cirrhosis between 4 to 6 years and in this group 1 patient was without AD, 4 had early AD and other 3 had definite AD. In group of 7 patients with duration of LC between 7 to 9 years, 1 patient had early AD, 1 patient had severe AD and remaining 5 patients had definite AD. Total 6 patients were known case of LC for more than 9 years, among them 2 patients had definite AD and 4 patients had severe AD.

**Table 1: Severity of AD and its correlation with Mean duration of LC**

AD severity group	Duration of cirrhosis				
	<1 year	1-3 years	4-6 years	7-9 years	>9 years
Normal	5	2	1	0	0
Early	3	13	4	1	0
Definite	0	1	3	5	2
Severe	0	0	0	1	4
Total	8	16	8	7	6

Out of 45 patients, 8 (18%) patients were not having AD. Out of 37 (82%) patients with AD, 32(71%) patients were having only parasympathetic dysfunction while remaining 5(11%) patients were having combination of sympathetic dysfunction and parasympathetic dysfunction.

**Table 2: Pattern of AD in LC**

Pattern of AD	No. of patients
Normal	8
Only parasympathetic dysfunction	32
Sympathetic and parasympathetic dysfunction	5

## DISCUSSION

Cirrhosis is defined as widespread fibrosis and nodule formation. In contrast Congenital hepatic fibrosis results in fibrosis without nodules. Partial nodular transformation is not a cirrhosis per se since it consists of nodules without fibrosis. The most common diseases lead to cirrhosis include chronic viral hepatitis, non-alcoholic fatty liver disease and chronic autoimmune biliary disease.<sup>7</sup> Alcoholic liver disease and hepatitis C are the predominant causes of cirrhosis in Western and European countries, whereas the prevalence of hepatitis B-induced cirrhosis is vastly increasing in developing countries. Hence, this study was conducted to study autonomic dysfunction in liver cirrhosis.

In the present study, 8 patients were diagnosed with LC within a year, out of which 5 patients were without AD and 3 patients had early AD. Total 16 patients were diagnosed with LC for more than 1 year but less than 3 years. Among them 2 patients were without AD, 13 patients had early AD and 1 patient had definite AD. 8 patients had duration of liver cirrhosis between 4 to 6 years and in this group 1 patient was without AD, 4 had early AD and other 3 had definite AD. In group of 7 patients with duration of LC between 7 to 9 years, 1 patient had early AD, 1 patient had severe AD and remaining 5 patients had definite AD. Total 6 patients were known case of LC for more than 9 years, among them 2 patients had definite AD and 4 patients had severe AD. A study by Bhaurao et al, 55 out of 60 (92%) cases were found to have an abnormal result in one or more autonomic function tests.<sup>8</sup> Similar results were observed in the study conducted by Bajaj and Agrawal et al, where 16(80%) out of 20 patients (10 alcoholics and 10 non alcoholics) of cirrhosis had autonomic dysfunction.<sup>9</sup> A study done by Manisha et al. showed almost similar results with 80% prevalence of Autonomic Dysfunction.<sup>10</sup> All these studies show prevalence of AD similar to present study.

In the present study, Out of 45 patients, 8 (18%) patients were not having AD. Out of 37 (82%) patients with AD, 32(71%) patients were having only parasympathetic dysfunction while remaining 5(11%) patients were having combination of sympathetic dysfunction and parasympathetic dysfunction. Another study by Franco Trevisani, Twenty-four (80%) patients showed AD, out of which vagal dysfunction was found in 19 patients (63%) and a sympathetic dysfunction in 7 (23%) patients.<sup>11</sup> In the study done by Bhaurao et al, only parasympathetic

dysfunction was found in 44(73.3%) cases while only sympathetic dysfunction was seen in 2(3.3%) cases.<sup>8</sup> 9(15%) out of 60 had combined sympathetic and parasympathetic dysfunction. In the study by Bajaj et al, only parasympathetic dysfunction was seen in 40%, combined sympathetic and parasympathetic dysfunction was seen in 40%, while no patient had isolated sympathetic dysfunction.<sup>9</sup>

Gentile et al.<sup>12</sup> found autonomic neuropathy in 71% patients of the alcoholic group and 57% of the non-alcoholic group out of total 113 patients with liver cirrhosis. In the study done by Hendrickse and Triger et al, cardiovascular autonomic dysfunction occurred with equal frequency in alcoholic (26/49; 53%) and nonalcoholic liver disease (26/55; 47%) and occurred in all the major groups of liver disease studied (primary biliary cirrhosis (18/28) 64%, alcoholic liver disease (26/49) 53%, autoimmune chronic hepatitis (5/16) 31%).<sup>13</sup>

## CONCLUSION

Severity of autonomic dysfunction increase with duration of liver cirrhosis. Parasympathetic dysfunction develops early in patients with liver cirrhosis accompanied by sympathetic dysfunction in advanced cases.

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