

# Women with Cirrhosis

## Prevalence, Natural History, and Management



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### KEYWORDS

- Women's health • Cirrhosis • Pregnancy • Hepatitis B • Hepatitis C
- Alcoholic Liver Disease • Nonalcoholic Fatty Liver Disease • Portal Hypertension

### KEY POINTS

- Cirrhosis is less frequent in women than in men, in large part due to the lower prevalence of hepatitis B, hepatitis C, and alcohol use/abuse in women.
- The most common causes of cirrhosis in women are hepatitis C, autoimmune etiologies, nonalcoholic steatohepatitis, and alcoholic liver disease.
- For most liver diseases, fibrosis progression appears to be slower in premenopausal women than in men, but with rates of progression equalizing in postmenopausal women.
- Women are at lower risk of hepatocellular carcinoma and have better outcomes than men following diagnosis.
- Pregnancy in women with cirrhosis is rare, as fertility is reduced and associated with high risk of complications.

### INTRODUCTION

Cirrhosis is an important public health concern in the United States. In a recent analysis of the National Health and Nutrition Examination Survey (NHANES) data conducted between 1999 and 2010, the prevalence of cirrhosis in the United States was approximately 0.27%, corresponding to 633,323 adults.<sup>1</sup> Women represented 27% of those adults. This lower prevalence of cirrhosis in women is closely related to their lower prevalence of hepatitis B virus (HBV) and hepatitis C virus (HCV) infections,<sup>2,3</sup> alcohol dependence,<sup>4</sup> and iron overload. It is still unsettled if nonalcoholic steatohepatitis is more prevalent in women than in men.<sup>5</sup> The most common causes of cirrhosis

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among women in the United States are HCV, autoimmune etiologies, nonalcoholic steatohepatitis, and alcoholic liver disease<sup>6,7</sup> (Table 1).

With increasing focus on a more personalized approach to care, knowledge of sex differences in liver disease prevalence, natural history, and treatment is important to optimize individual long-term outcomes. Additionally, there are unique issues in managing women with advanced stages of fibrosis with regard to conception, pregnancy, and postpartum care.

## SEX DIFFERENCES IN THE NATURAL HISTORY OF SPECIFIC LIVER DISEASES

### Chronic Hepatitis C

Globally and especially in North America, chronic HCV is a major cause of cirrhosis, hepatocellular carcinoma, and liver-related mortality (Table 2).<sup>8,9</sup> The natural history of HCV has consistently been shown to be different in women compared with men. Spontaneous clearance of the virus occurs more frequently among women than men. In a recently published collaboration of 9 prospective cohorts of HCV-infected patients, 37% of women with acute HCV infection cleared the virus, whereas only 21% of men did so.<sup>10</sup> Female sex is also a protective factor for the progression of liver fibrosis in premenopausal but not postmenopausal women with HCV, believed to reflect the protective effect of estrogens. In an analysis of 157 women with HCV (61 premenopausal and 96 postmenopausal), postmenopausal women had higher mean fibrosis scores than premenopausal women ( $1.87 \pm 0.16$  vs  $1.17 \pm 0.10$ ;  $P < .01$ ) and rates of fibrosis progression ( $119 \pm 5$  vs  $93 \pm 12 \times 10^{-3}$  METAVIR units/y;  $P < .05$ ).<sup>11</sup> Moreover, among postmenopausal women, there was less advanced fibrosis in those who had received hormone replacement therapy compared with those who had not ( $1.79 \pm 0.25$  vs  $1.93 \pm 0.20$ ;  $P < .05$ ) and slower rate of fibrosis progression ( $99 \pm 16$  vs  $133 \pm 6 \times 10^{-3}$  METAVIR units/y;  $P = .02$ ). In addition to the potential fibrosis-modifying effect of sex hormones, other factors contributing to a lower rate of advanced liver disease in women compared with men include the lower frequency of cofactors associated with accelerated disease progression, like alcohol use and human immunodeficiency virus infection.<sup>12,13</sup> In a study of 376 young Irish women who contracted HCV in 1977 and 1978 from contaminated anti-D immune globulin, only 1.9% had probable or definitive cirrhosis after a follow-up of 17 years.<sup>14</sup> A similar German cohort study of 1980 women who contracted HCV in 1978 to 1979 from contaminated anti-D immune globulin showed that after 25 years, only 9 patients (0.5%) had cirrhosis and 1 hepatocellular carcinoma (HCC) was diagnosed.<sup>15</sup> Comparatively, an analysis of the Electronically Retrieved Cohort of HCV Infected Veterans (92.9% men), in which HCV-positive patients were identified with an initial

**Table 1**  
Common causes of cirrhosis in women versus men

Patient Type and Country	Women <sup>a</sup>	Men <sup>a</sup>
Cirrhosis estimated by population-based study (England) <sup>7</sup>	Alcoholic liver disease	Alcoholic liver disease
	Cryptogenic	Cryptogenic
	Autoimmune	Viral hepatitis
	Viral hepatitis	Autoimmune
Cirrhosis estimated by those on waiting list for transplantation (US) <sup>6</sup>	Viral	Viral
	Autoimmune etiologies	Alcoholic liver disease
	Nonalcoholic fatty liver disease	Nonalcoholic fatty liver disease
	Alcoholic liver disease	Autoimmune etiologies

<sup>a</sup> Listed from most prevalent to less prevalent.

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