

## Role of Cirrhosis A Review Article

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**Abstract:** - When cell are injured or damaged and die off usually that dead tissue that was previously full of living cells becomes fibrotic meaning it become thickened with heaps and heaps of protein and form scar tissue so when your liver is constantly forced to process alcohol like an alcoholic liver disease or subject to a viral attached for a long time like a virus ( HBV or HCV) or anything else that cause a long term or chronic state of liver cell or hepatocytes destruction and inflammation your liver can become seriously Scarred and damage to the point where it's no longer reversible at which point it's became fibrotic and in the liver we call this process cirrhosis.

**Keyword:** - cirrhosis; stellate cell; transforming growth factor- $\beta$  (TGF- $\beta$ ); portosystemic shunt

### Introduction:

Because it usually irreversible cirrhosis. Cirrhosis is often referred as “end stage” or “late stage” liver damage [1]. When liver cell injured they start to come together and form what are call generative nodules. You can think of these as colonies of living liver cell these are one of the classic sign of cirrhosis and that why cirrhotic liver is more bumpy as opposed to a smooth healthy liver also with

cirrhotic liver tissue. You will see that in-between theses clumps of cell or nodules is fibrotic tissue and collagen there is a classic historical image of a cirrhosis tissue (figure 1). This clump of cell in the middle is the regenerative nodules and these blue stains surrounding it are the band of protein from the process of fibrosis. If we zoom out in a bit and Look at it with the naked eye we will again see these nodules which have fibrotic protein band in between (figure 2).

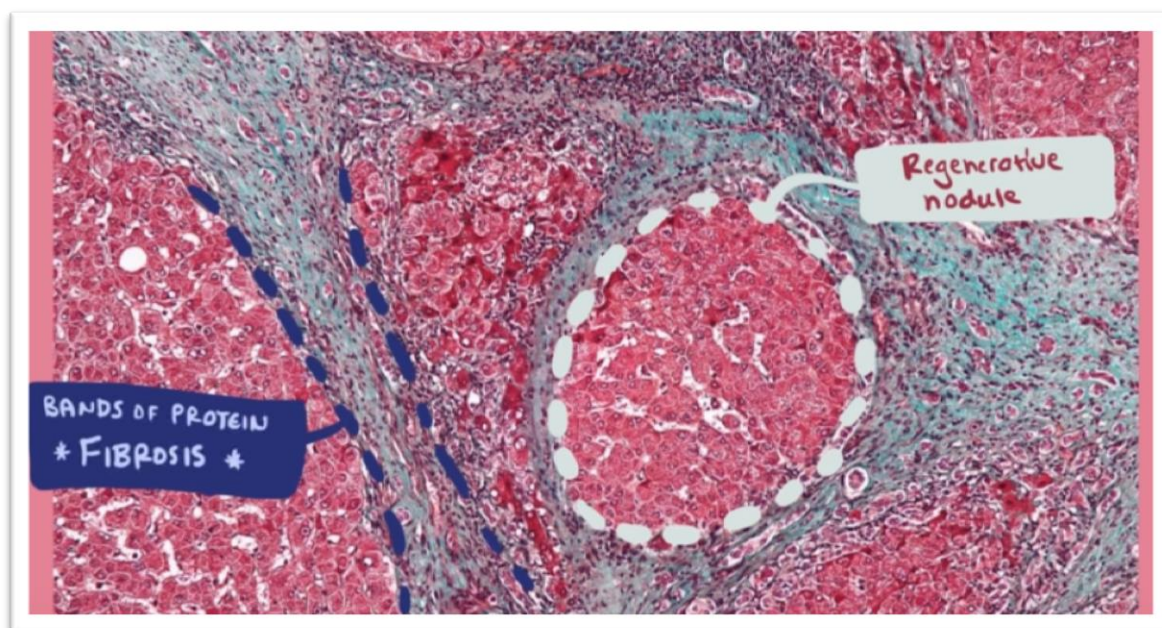
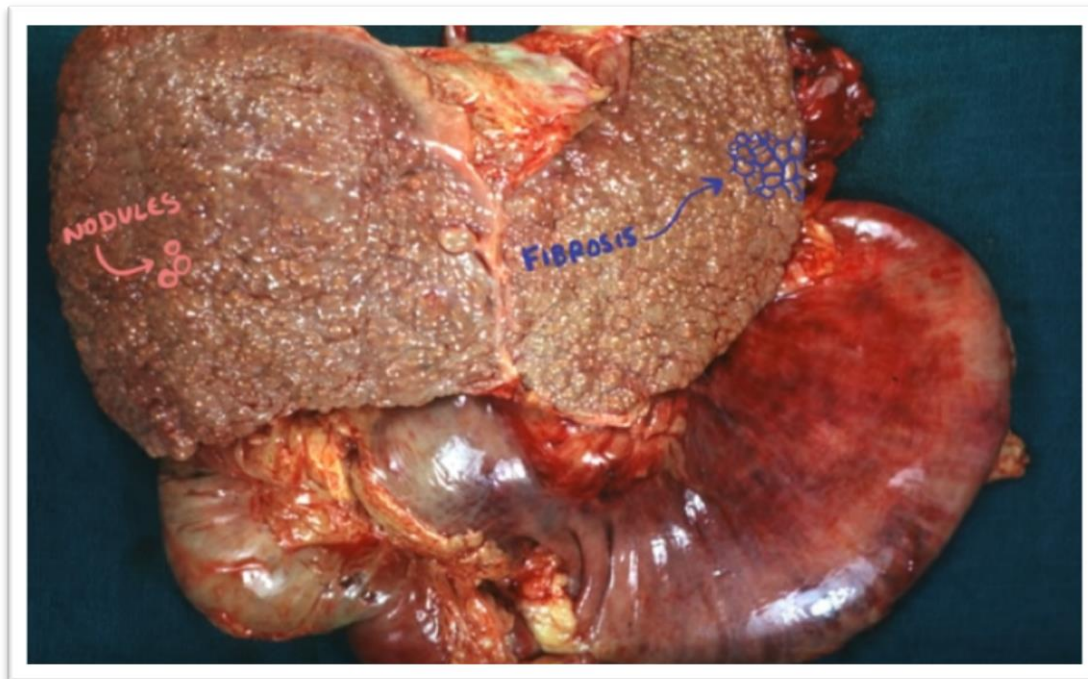


Figure 1:- Classic histology image of cirrhotic tissue



**Figure 2:-** Nodules and fibrotic protein band

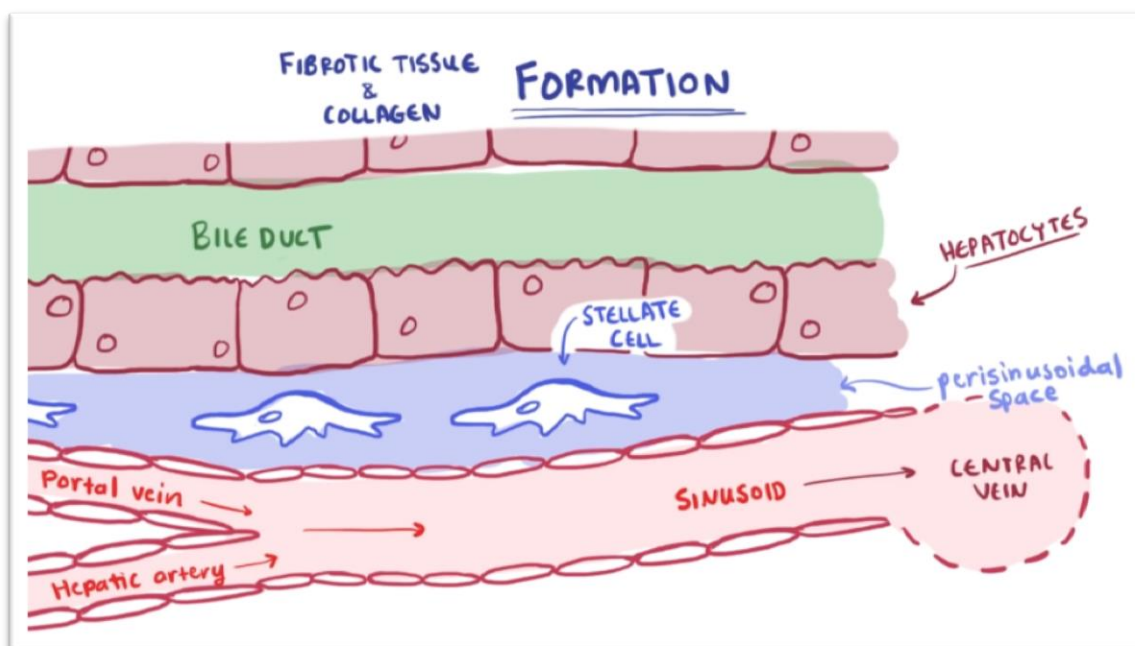
### **Discussion:**

Alright but how do these band fibrotic tissues form? Well fibrosis is a process mediated by these special cells called stellate cells that sit between the sinusoid and hepatocyte known as the perisinusoidal space. Here is a pretty basic layout of the basic functional unit of a liver. You have got the portal vein in the hepatic artery that combined into a sinusoid which then goes into the central vein these are all aligned with hepatocytes. Along this though you have also got a bile duct and all these three constitute a portal triad so the perisinusoidal space, which literally means around the sinusoidal space and stellate cell (figure 3) [2, 3]. And usually in healthy tissue these guys' main function is to store vitamin A and are otherwise considered quiescent or sort of dormant when the hepatocytes are injured though they secrete paracrine factors that activate and sort of change the stellate cells when activated these stellate cells lose vitamin A, proliferate and start secreting transforming growth factor beta 1 or secrete Transforming growth factor- $\beta$  (TGF- $\beta$ ) which then cause them to produce collagen which is the main ingredient in extracellular matrix fibrosis [4] and then scar tissue as this fibrotic tissue builds up. It starts to compress the central vein and sinusoid. It is though that in a healthy normal state these stellate cells play a key role in a natural wound healing process,

but when the liver cells are constantly injured, the stellate cells are constantly activated and so they constantly produce collagen and factors that lead to fibrosis [3]. And this is when complication due to cirrhosis starts to crop up, as those central veins and sinusoids become compressed and push on the fluid inside, the pressure starts to build up, leading to intrastellate sinusoidal or sometimes called portal hypertension [5]. Which is this higher pressure in the portal vein, higher portal vein pressure means that fluid in the blood vessels is more likely to get pushed into tissue and across the tissue into the large open space like the peritoneal cavity. That's why cirrhosis leads to excess peritoneal fluid, a condition called ascites [15]. And can result in complications like congestive splenomegaly and hypersplenism [6, 7], where the spleen becomes enlarged because all this fluid and blood cannot get into the liver, and backs up into the spleen instead in the same way or circulatory system starts diverting blood away from the liver because of the high liver pressure and this is known as a portosystemic shunt [5]. And this happens because blood flow follows the path of least resistance and basically shunts away from the portal system and towards the systemic system of circulation through not fully understood changes in a portal flow ultimately trigger renal vasoconstriction so

increased resistance in the renal circulation which decrease of blood flow through the kidney leading to decreased filtration and hepatorenal failure where kidney failure follows liver failure. the fibrotic tissue pressure build up and diversion of a blood from the hepatic circulation essentially reduce the number of functional sinusoidal Veins and the number of functional portal triad is generally, as you have less and less of this basic liver functional unit your need your liver becomes less and less this able to do its job of detoxification .when the liver isn't detoxifying the blood these toxins can get into the brain and start causing mental deficits a condition known as hepatic encephalopathy. Although there are several neurotoxins that are through to contribute to the development these mental changes the best understood factors is ammonia in the blood. Which is produced mainly in the gastrointestinal tract. Usually the liver plays a huge role in removing ammonia and stopping it from going in the systemic circulation. as the liver become more damaged these and other toxins get into the brain and patient might develop asterixis where they have tremors or jerking hand when outstretched .and is even more toxins build-up eventually patient can progress to a coma, also since the liver play a big role in metabolizing estrogen into inactive metabolites that can be removing from the blood and excreted patient can also experience complication due to increased estrogen in the blood

like gynecomastia , spider angiomas and Palmar erythema and since the liver usually conjugates bilirubin they will be increased unconjugated bilirubin in the blood from a less functional liver and that can be lead to jaundice [8].another important jobs of the liver is produce albumin. So again If the liver is not functioning. You can have a decreased amount of albumin in the blood or hypoalbuminemia. Finally the liver help in making clotting factors or protein that helps coagulate your blood. So when you aren't producing these coagulation factors you can develop issues related to your ability to conjugate blood. Which you need to in order to stop blood loss after an injury. so to recap the general symptoms of cirrhosis includes compensated and decompensated stages[9], early on with a small amount of scarring in Fibrosis. we call it compensated cirrhosis meaning that the liver can still do a lot of its job in this case somebody with the cirrhosis might not have any symptoms or they might have none specific symptoms like weight loss, weakness or fatigue. later on though with extensive scarring and the liver progress to decompensated cirrhosis and it can't function normally at this point a lot of the describe symptoms start to develop like a jaundice and pruritus (itchy skin), ascites, hepatic encephalopathy which can lead to confusion and easy bruising from the localization factor[10].



**Figure 3:-** Formation of fibrotic tissue and collagen

### **Diagnosis:**

Gold standard is a liver biopsy which is taking a tiny sample of the liver tissue and examining it under a microscope[7, 11] and common lab finding including elevated serum bilirubin as well as elevated liver enzyme like \* aspartate aminotransferases (AST) \*alanine aminotransferase (ALT) ,AST is usually more elevated than ALT and also \*alkaline phosphatase (ALP) and, \*gamma glutamyltransferase (GGT) can also be elevated[10, 12] and might be thrombocytopenia or low platelet count[13].

### **Treatment:**

Generally the scarring in cirrhosis is the irreversible so first of all it's important to prevent continued liver damage by identifying the underlying underlining causes in treating. that for example:- stopping alcohol consumption or antiviral treatment for hepatitis c[9] with advanced cirrhosis though where the liver stop functioning a liver transplant might be needed[1, 14] .

### **Conclusion:**

Cirrhosis is when the inflammation and liver damage cause the liver to become fibrotic and develop scar tissue. cause include things likely excessive alcohol consumption or prolonged viral attack like a from hepatitis b and hepatitis c virus over time as the liver become less functional symptoms is like jaundice, ascites, easy bruising and hepatic encephalopathy develops. Diagnosis is often done within the biopsy and / or lab test. And treatment for advanced cirrhosis is to treat at the underlining causes but sometimes a liver transplant required.

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### **Conflicts of interest:**

The authors declare no conflicts of interest.

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