

## CONCLUSIONS

Based on the results of the present study, it can be concluded that:

- Patients with HCV-related liver disease showed increased serum mTOR levels and intrahepatic mTOR expression suggesting that the mTOR pathway is activated during chronic HCV infection.
- The direct correlation between mTOR levels in sera and livers and the enhanced inflammatory response, progression of fibrosis and development of steatosis in HCV-infected livers may suggest that mTOR activation is implicated in the pathogenesis of HCV-induced liver injury and fat accumulation in the liver.
- The development of HCC in patients with HCV-related liver disease was associated with a further significant increase in mTOR levels in sera and tumor tissues which were positively correlated with tumor progression. These findings indicate that mTOR pathway plays a critical role in HCV-associated hepatocarcinogenesis.
- Serum mTOR levels showed a high sensitivity and specificity in discriminating cirrhotic patients with and without HCC and could represent a potential diagnostic biomarker for the development of HCC in chronic HCV infection.
- Dysregulation of autophagy was observed in patients with chronic HCV infection and was inversely correlated with hepatic necroinflammation and fibrosis suggesting that autophagy has anti-inflammatory and anti-fibrotic effects.
- The fact that autophagy was markedly inhibited in patients with HCV-related HCC, may suggest that autophagy functions as tumor suppressor mechanism and a down-regulated autophagy may contribute to the development and progression of HCC.
- The inverse correlation between mTOR activation and autophagy indicates that mTOR is a negative regulator of autophagy and may utilize autophagy inhibition as a mean to promote HCV-related liver injury and HCC development.
- The finding that autophagy was induced in HCV-infected hepatocytes despite mTOR activation in some patients may suggest that autophagy inducers have overcome the suppressive effect of mTOR on autophagy in HCV-infected cells.
- Altogether, the results of the present study suggest that chronic HCV infection is associated with activation of mTOR pathway which may play a role in HCV-related liver injury and in the development and progression of HCC, possibly, through inhibition of autophagy.