Summary

There are 170 million people worldwide with persistent hepatitis C virus (HCV) infection that are at significant risk of progressive liver injury leading to cirrhosis, death from liver failure, and hepatocellular carcinoma. **(Liang TJ, et al; 2000; Lauer GM& Walker BD,2001).** Currently standard treatment includes a combination of sofosbuvir, pegylated interferon (peg-IFN) and ribavirin. A substantial proportion of patients infected with HCV still do not respond to sofosbuvir, peg-IFN/ribavirin therapy,therefore predictive factors that identify potential non responders are needed to limit drug exposure in patients unlikely to benefit from treatment and to save healthcare resources.

Our study included one hundred non-diabetic, non-cirrhotic Egyptian patients with chronic HCV infection. Study included 55 males (55%) and 45 females (45 %) their ages ranged from (25-48) years. Patients then divided in two groups according to type of treatment which they received.

Group (I): 50 cases treated with standard treatment (pegylated interferon plus ribavirin) for 48 weeks.

Group (II):50 cases treated by new regimen (sofosbuvir,pegylated interferon plus ribavirin) for 12 weeks.

Each group was further sub divided in two groups according to insulin resistence **(HOMA- IR).**

Group (I)	Group (A): 25 cases with HOMA –IR Less than 2.
	Group (B): 25 cases with HOMA –IR more than 2.
Group (II)	Group (C): 25 cases with HOMA –IR Less than 2.
	Group (D): 25 cases with HOMA –IR more than 2.

Our aim was to identify the role of insulin resistance as a disease modifier affecting progression of liver fibrosis and sustained virological response in chronic HCV infection and effect of SVR on insulin resistence.

In our study.by Studying the impact of IR on SVR, we found statistical significant difference in the SVR between patients with IR < 2 and patients with IR> 2 in group one treated by old regimen pegylated interferon&ribavirin but no statistical significant difference in the SVR between patients with IR < 2 and patients with IR> 2 in group two treated by new regimen pegylated interferon,ribavirin&sofosbuvir.

In our study we found a direct correlation between IR an BMI in all patients.There is inverse relationship between BMI&SVR in patients treated by pegylated interferon&ribavirin but had no effect on patients treated by sofosbuvir,interferon&ribavirin.

Also in our study we found a direct correlation between IR and liver steatosis.but not with necroinflammation or liver fibrosis which had negative impact on SVR in patients treated by old regimen pegylated interferon &ribavirin but had no effect on SVR in patients treated by new regimen sofosbuvir,interferon&ribavirin.

As regarding pretreatment viral load in our study we found that it is not a predictor of SVR in all patients.

In our study also pretreatment ALT is not a predictor of response to SVR in both groups.

In our study we found significant improvement in insulin resistence in both groups after the end of treatment .This means that HCV therapy, regardless of achievement of SVR, appeared to improve IR.

conclusion

1- when using precise measurements of IR, IR appear to have negative impact on achievement of SVR in patients treated by old regimen pegylated interferon &ribavirin but had no effect on SVR in patients treated by new regimen sofosbuvir,interferon&ribavirin.

2-we found a direct correlation between IR and BMI and steatosis in all patients.There is inverse relationship between BMI,steatosis&SVR in patients treated by pegylated interferon&ribavirin but had no effect on patients treated by sofosbuvir,interferon&ribavirin.

3- Successful viral eradication did not appear to substantially influence IR when compared with HCV therapy that does not result in SVR. However, HCV therapy, regardless of achievement of SVR, appeared to improve IR. This suggests that individuals with higher degrees of IR may benefit from receipt of HCV therapy in an attempt to decrease their risk of clinical sequelae of IR.This study highlights the potential limitations of use of surrogate measures of IR within the context of HCV therapy by new regimens sofosbuvir,prgylated interferon&ribavirin.