Aim: Alpha-fetoprotein (AFP) has been widely used as a diagnostic marker for hepatocellular carcinoma. Some patients with hepatitis C show high AFP values, but no evidence of hepatocellular carcinoma. The aim of this study is to assess the influence of antiviral treatment on the serum AFP in patients with chronic hepatitis C without hepatocellular carcinoma. Material and Method: Thirty seven chronic hepatitis C patients (20 females and 17 males) were included in the study. All patients were given a combined treatment of pegylated or conventional interferon (IFN) and ribavirin. Serum AFP was measured at baseline and on months 3-6-12 of the therapy. Results: Compared to the pretreatment levels of ALT (88.59 ± 57.22 IU), those at 3, 6 and 12 months were statistically lower (p< 0.001). Mean serum AFP levels gradually decreased from pretreatment level of 6.6 ± 6.05 ng/ml to 5.1 ± 3.7 (p>0.05), to 4.34 ± 4.64 (p>0.05) and to 2.63 ± 2.17 (p<0.001) at month 3, 6 and 12 of the therapy, respectively. Although AFP decrease at month 3 was non significant, a significant decrease of mean serum AFP levels after 6 and 12 months of therapy was demonstrated in the patients with high AFP (>10 ng/ml). In these patients, mean serum AFP levels were decreased from pretreatment level of 15.09 ± 5.92 ng/ml to 11.39±3.30, to 6.97±2.53 (p<0.001) and to 5.67±3.89 (p=0.009) at month 3, 6 and 12, respectively. Discussion: Serum AFP level significantly decreases during therapy in hepatitis C patients receiving IFN-α plus ribavirin for 48 weeks.