Reviewer 1:

Specific Comments to Authors: In their report, the authors assessed the role of circulating miRNAs326, miRNA-424 and miRNA-511 in Egyptian HCC patients.
They show that miRNAs326, miRNA-424 and miRNA-511 could have diagnostic and prognostic roles in Egyptian HCC patients and should be considered for better management of the disease. However,
the similar results were reported in several papers, including PMID: 28060739, PMID: 26927063. Therefore, the current status of the manuscript is not full of sufficient novelty, and not meet the criteria of a high quality World Journal of Gastroenterology paper.

Reply:

Dear Sir;
First, thank you for your valuable comments and kindly find answers below:

In the first original article: **Lu M, Kong X, Wang H, Huang G, Ye C, He Z.** A novel microRNAs expression signature for hepatocellular carcinoma diagnosis and prognosis. Oncotarget. 2017 Jan 31;8(5):8775-8784. doi: 10.18632/oncotarget.14452. PMID: 28060739

They investigated miRNA in Chinese population most probably with HCC secondary to HBV, although they did not mention the underlying etiology of their patients whether HCV, HBV or NASH

They mentioned in their discussion part that: "To their disappointment, they did not find the association between miRNAs signature and HBV/HCV, or AFP, or other routine biomarkers. It suggested that there are some differences between the western and eastern countries in terms of tumorigenesis and tumor progression of HCC. Chinese patients are mainly infected with HBV whereas most US patients usually carry HCV instead. "

Moreover, this study was carried out on tissue samples, which is invasive and very hard to obtain, while in our study, we tested miRNA from plasma as a noninvasive route.

While the second mentioned review article: **Hayes CN, Chayama K.** MicroRNAs as Biomarkers for Liver Disease and Hepatocellular Carcinoma. Int J Mol Sci. 2016 Feb 24;17(3):280. doi: 10.3390/ijms17030280. PMID: 26927063; PMCID: PMC4813144.

They mentioned that microRNA profiles differ in the case of HBV and HCV infection as well as between HBeAg-positive and negative patients, and in patients with occult versus active HBV infection.

Our study is the first to be done in Egyptian patients with the single etiology of HCV-related HCC. We have HCV genotype 4 in Egypt responsible for over 94% of cases.

Besides, none of the studied miRNA was discussed in this review article.

Reviewer #2:

Specific Comments to Authors: This is an interesting paper presenting the prevalence and potential role of three different MiRNAs regarding HCC in an Egyptian population.

1) **Why did the authors choose only patients with HCV related liver cirrhosis?**

We chose these patients as HCV is the most common cause of chronic liver disease in Egypt. We excluded patients without single HCV infection of the liver to study the changes in microRNAs in patients with the single etiology of HCV-related HCC. As miRNA profiles differ in the case of HBV and HCV infection.

Hayes CN, Chayama K. MicroRNAs as Biomarkers for Liver Disease and Hepatocellular Carcinoma. Int J Mol Sci. 2016 Feb 24;17(3):280. doi: 10.3390/ijms17030280. PMID: 26927063

2) Also for controls did the authors consider patients with cirrhosis but without HCC and also patients with HCC but without cirrhosis?

As we intended to include patients with the single etiology HCV-related HCC, all the patients had HCC on top of liver cirrhosis, As HCC usually develops on top of liver cirrhosis in patients with HCV.

Unfortunately in the control group we included only healthy patients.

3) What kind of HCV treatment had those patients received currently and in the past?

These patients did not receive antiviral treatment for HCV

4) The authors, given the fact that all their patients were HCV-HCC, should perhaps rephrase the conclusion so that it has to do with the specific subset of patients

This was corrected in the conclusion of the abstract and in the discussion part

5**) What treatments did these patients receive?**

All our patients were HCC-treatment naïve at the time of enrollment

As we mentioned in the results section: According to the BCLC staging system, most of the patients were in the early stage (48.6%). Most of the HCC lesions were single (70%), present in the right hepatic lobe (84.3) and not associated with portal vein thrombosis (92.9%) that's why most of the patients were subjected to hepatectomy and Microwave ablation (MWA)