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USING MIRNA-185 AS BIOMARKERS FOR DIAGNOSIS CHRONIC HEPATITIS B VIRUS INFECTION IN AL-DIWANIYAH CITY, IRAQ

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ABSTRACT

Chronic hepatitis B virus (HBV) infection continues to be a fairly global health challenge, especially in high-reach areas, such as al-Diwaniya City, Iraq. The purpose of this study is to identify chronic HBV infections, evaluate their clinical accuracy and to investigate their correspondence with clinical and demographic factors as a new biomarker to check the capacity of the microRORNA, especially the MIRNA-185. The study included 80 samples, including 40 chronic HBV patients and 40 in healthy controls, match age and gender. Demographic and clinical data were collected, including age, gender, smoking conditions and alcohol intake. We did the liver function test (Alp, GOT, GPT and TSB) to see if there was any damage to the liver. We took RNA from blood tests and used stem-loop reverse transcription Quantitative PCR (RT-QPCR), which was a very sensitive and specific approach to detect Mirna to measure the level of MIRNA-185. Demographic and clinical variables were investigated, including smoking (45% patients against 32.5% control, $p = 0.251$) and alcohol intake (25% patients against 7.5% control, $p = 0.034$). Liver function tests (LFTs) indicated significant increases in alkaline phosphatase (ALP, 358.2 ± 37.01 vs. 94.05 ± 14.6 IU/L, $p = 0.001$), aspartate aminotransferase (GOT, 73.3 ± 12.5 vs. 31.00 ± 5.08 IU/L, $p < 0.001$), alanine aminotransferase (GPT, 107.4 ± 18.6 vs. 22.15 ± 4.6 IU/L, $p < 0.001$), and total serum bilirubin (TSB, 1.45 ± 0.44 vs. 0.35 ± 0.08 mg/dL, $p < 0.001$) in HBV patients compared to controls. The miRNA expression analysis indicated substantial dysregulation of both miRNAs in chronic HBV patients relative to controls. miRNA-185 was significantly overexpressed (mean ± SE: 11.01 ± 1.29 vs. 1.18 ± 0.12 in controls, $p < 0.001$). The Receiver operating characteristic (ROC) analysis analysis showed that the MIRNA -185 was very good in diagnosis, with a region under a curve (95%CI: 0.925–1,000), sensitivity of 97.5%, a specificity of 95.0%, a positive prediction (PPV) of 95.0%. > 2.86-Guuna. Finally, our study provides sufficient evidence that supports the use of MIRNA-185 as a clinical biomarker for chronic HBV infection in the city of Al-Diwaniya. Clinical practice has the ability to support the early detection of the inclusion, increase the patient's results and support the global initiative to reduce the effect of HBV -related liver disease.

KEYWORDS: Chronic hepatitis B virus, miRNA-185, ALP, GOT, GPT, RT-qPCR.

INTRODUCTION

Chronic hepatitis B virus (HBV) infection is a major health problem worldwide, especially in areas with high areas such as al-Divashali City, Iraq. The World Health Organization (WHO) estimates that there are over 257 million people around the world, which has an old HBV infection. Most of them live in the Asia-Pacific region and Africa Underby.[1] It is believed that about 2-7% of people in Iraq have chronic HBV infections. In some places there are high prices, such as al-Divanih City.[2] An early and correct identity of chronic HBV is very important for good disease management and to avoid results such as cirrhosis and hepatosol carcinoma (HCC). Traditional clinical techniques, which include serological markers (eg hepatitis B surface antigen, HBSAG) and liver function test (LFT), often show insufficient sensitivity and specificity for initial diagnosis and immunity evaluation.[3.4] In addition, this traditional function can make the complex pathophyziology of chronic HBV infection inadequate clearly, characterized by complex host-host virus interaction and dynamic disease development.[5.6] Recently, Mirnaer has become interesting biomars' for many liver diseases, such as chronic viral hepatitis.[7.8] Mirna is small, non-coding

RNA molecules that are very important for regulating gene expression by transcription. They change cellular processes that are very important for the development of HBV.[9,10] Some MIRN's indigestion has been linked to different stages of chronic HBV infections, from the first viral input to the beginning of HCC.[11,12] Among the MIRNAs associated with HBV-related liver disease, the MIRNA-185 has attracted considerable attention. The MIRNA-185 is a heavily protected microNA involved in various physiological processes, including cell proliferation, death and immunological modulation.[13,14] In the installation of chronic HBV infection, the MIRNA-185 has been identified as an excessive increase in infected individuals, reflecting its potential participation in viral replication and immune theft.[15,16] It is believed that Viral Oncoprotein HBX has a role in over-expression of MIRNA-185 in old HBV patients. This is because HBX has proven to interact and change with expressions of different hosts Mirna.[17,18] HBX is a multidisciplinary protein that is very important in the development of HBV. It is believed that its ability to disrupt the host's mirna network is an important way that the virus can avoid the protective reactions and live and reproduce.[19,20] The unique manifestation pattern of MIRNA-185 in chronic HBV infection indicates its ability as a viable biomarker characterized by a viable biomarker for diagnosis of the disease and the diagnosis of the disease. In addition, the functional importance of MIRNA-185 in HBV-Patogenesis, especially viral replication and its role in immunoth, provides a compelling measure of potential treatment strategies.[21,22] The study wants to examine the effect of MIRNA-185 as a new biomarker for diagnosis of chronic HBV infection in the city of Al-diwaniya in Iraq. The project will evaluate the clinical accuracy of MIRNA-185 and examine its correlation with clinical indicators and demographic factors, aimed at the use of it in chronic HBV care.

MATERIALS AND METHODS

Study Design and Participants

This case control study was performed from October 1, 2024 to March 1, 2025 in Al- diwaniya City, Iraq. The study population consisted of 80 people, including 40 patients with HBV infection and 40 healthy control age and gender.

Chronic HBV patients were detected to detect hepatitis B surface antigen (HBSAG) for a minimum period of 6 months, increased liver enzymes and specific clinical and radiological manifestations. Healthy controls were individuals with no known liver disease or viral hepatitis infection, which matched the patient chocolate by age and gender.

For all participants, demographic and clinical information such as age, gender, smoking conditions and alcohol were gathered. We conducted liver function tests to investigate for liver damage. These tests included alkaline phosphate (ALP), aspartataminotransferase (GOT), Eleinin Aminotransferase (GPT) and Total Serum Bilirubin (TSB). The institutional board of review authorized the study protocol, and all participants gave their written consent to participate.

RNA Extraction and miRNA Quantification

According to the manufacturer's instructions, we used a trizzo -rag setting to extract total RNA from blood tests. A nanodrop spectrophotometer was used to find out how clean and focused RNA was. Stem loop reverse transcription Quantitative PCR (RT-QPCR) was used to measure the levels of MIRNA-185. The STAM-LOOP RT-QPCR approach was used, which has two steps: (1) to transfer CDNA to MIRNA using the stem loop chips, and (2) to find and find the target MIRNA using (2) the quantitative PCR. This method is very specific and sensitive to measuring MIRNA levels. Gotaq® QPCR Master Mix Kit, who comes with SYBR Green Die to detect, was used to run a miniopticon to run the PCR reactions on the PCR machine in real time. We used the ΔCT method to find out how much the MIRNA-185 was expressed to the MIRNA-185 compared to GAPDH, which is an internal control.

Statistical Analysis

Continuous variables were displayed as mean ± standard deviation (SD) or median (range), where suitable. We used frequencies and percentages to show categorical variables. The independent t-test or the chi-square test, as needed, were used to compare groups.

We used receiver operating characteristic (ROC) curve analysis to find the best cutoff values for miRNA-185 based on the highest Youden's index. We found the area under the curve (AUC), sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV).

We employed Pearson's correlation analysis to look into how miRNA expression and clinical factors, such liver function tests, are related. We used SPSS software (version 25.0) for all of the statistical analyses, and a p-value of less than 0.05 was considered statistically significant.

RESULTS

Demographic and Clinical Characteristics

The study included 80 participants, with 40 chronic HBV patients and 40 age- and sex-matched healthy controls. The mean age of the study participants was 44.80 ± 11.81 years in the HBV group and 42.65 ± 10.14 years in the control group, with no significant difference ($p = 0.463$). The proportion of male participants was 60% in the HBV group and 75% in the control group, with no significant difference in the gender distribution between the two groups ($p = 0.152$). Regarding lifestyle factors, 45% of HBV patients were current smokers, compared to 32.5% in the control group, with no significant difference ($p = 0.251$). However, the proportion of alcohol drinkers was significantly higher in the HBV group (25%)

compared to the control group (7.5%, p = 0.034). As show in table (1) and (2).

Table 1: Comparison between patients and control groups in Age group.

Age	Chronic hepatitis B	Healthy control	Total	p-value
Mean ± SD	44.80 ± 11.81	42.65 ± 10.14		0.463 † NS
< 30 years, *n*	5 (12.5%)	8 (20.0%)	13 (16.3%)	0.373 ¥ NS
30-39 years, *n*	9 (22.5%)	12 (30.0%)	21 (26.2%)	
40-49 years, *n*	12 (30.0%)	6 (15.0%)	18 (22.5%)	
≥ 50 years	14 (35.0%)	14 (35.0%)	28 (35.0%)	

n: number of cases; **SD**: standard deviation; †: Independent T test; ¥: Chi-square test; N**S**: non-significant at *P* > 0.05

Table 2: Comparison between patients and control groups in gender.

Study groups	Gender		Total	p-value
	Male	Female		
Chronic hepatitis B	24 (60.0%)	16 (40.0%)	40	0.152 ¥ NS
Control	30 (75.0%)	10 (25.0%)	40	
Total	54 (67.5%)	26 (32.5%)	80	

¥: Chi-square test; **NS**: not significant at *P* > 0.05

Liver Function Tests

The HBV group exhibited significantly elevated levels of liver function tests compared to the control group. The mean ALP level was 358.2 ± 37.01 IU/L in HBV patients and 94.05 ± 14.6 IU/L in controls (p = 0.001). Similarly, the mean GOT level was 73.3 ± 12.5 IU/L in HBV patients and 31.00 ± 5.08 IU/L in controls (p < 0.001), and the mean GPT level was 107.4 ± 18.6 IU/L in HBV patients and 22.15 ± 4.6 IU/L in controls (p < 0.001). The total serum bilirubin (TSB) was also significantly higher in the HBV group (1.45 ± 0.44 mg/dL) compared to the control group (0.35 ± 0.08 mg/dL, p < 0.001). As show in table (3) and figure (1-3).

Table 3: Results of liver function tests (ALP, GOT, GPT and TSB) in patients and healthy controls.

Groups	ALP	GOT	GPT	TSB
Chronic hepatitis B	**358.2 ± 37.01**	**73.3 ± 12.5**	**107.4±** 18.6	**1.45±** 0.44
	217.00-484.0	31.00-154.00	46.00-188.00	0.20-3.43
Control	**94.05** ± 14.6	**31.00** ± 5.08	**22.15** ± 4.6	**0.35** ± 0.08
	58.0-119.0	17.00-44.00	13.00-33.00	0.18-0.51
p-value	**0.001****	**0.001****	**0.001****	**0.001****

SD: standard deviation; †: Independent T test ******: significant at *P* < 0.05

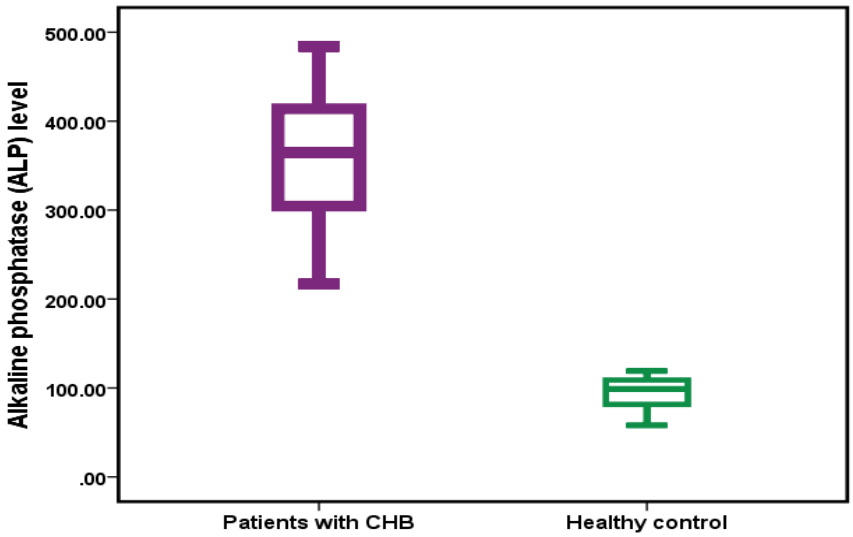

Figure (1): The means level of serum ALP in patients and control groups.

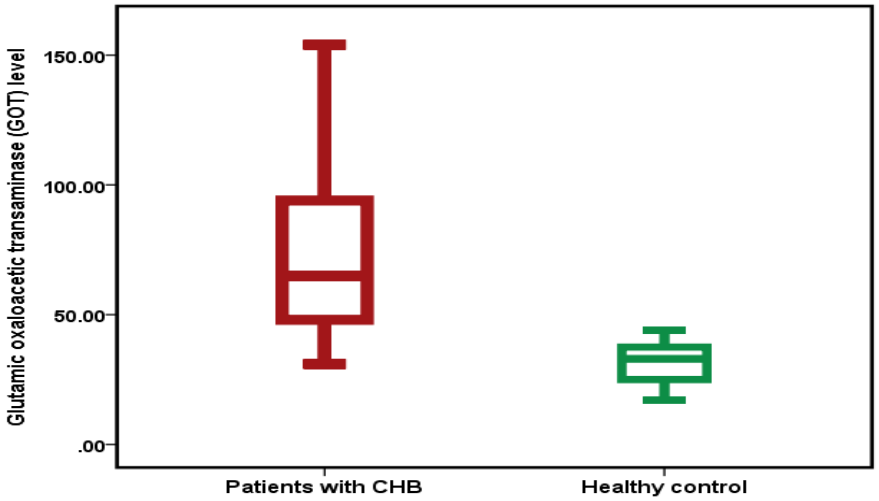

Figure (2): The means level of serum GOT in patients and control groups.

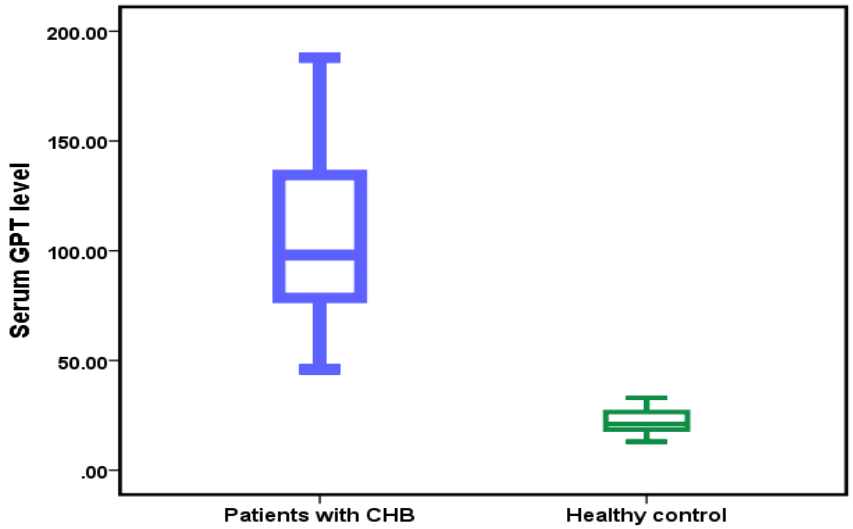

Figure (3-6): The means level of serum GPT in patients and control groups.

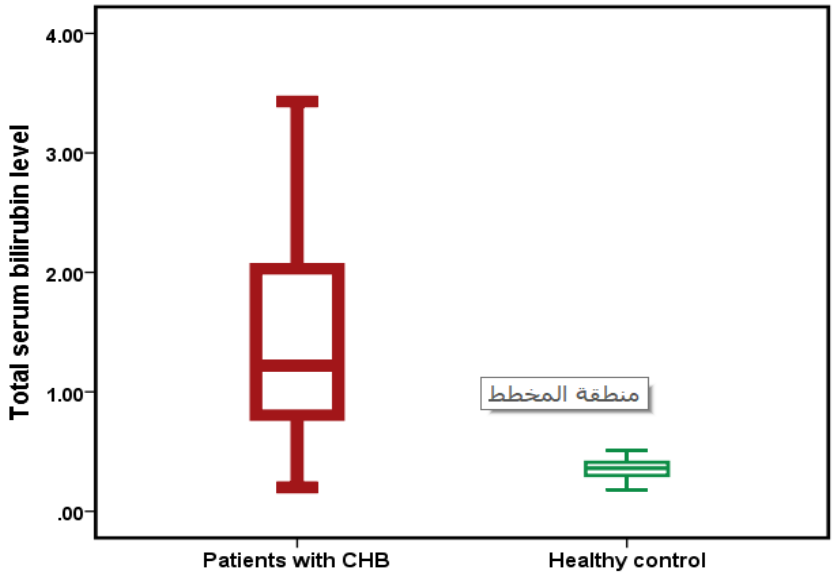

Figure (3): The means level of serum TSB in patients and control groups.

miRNA Expression

The expression levels of miRNA-185 were significantly dysregulated in chronic HBV patients compared to healthy controls. miRNA-185 was markedly overexpressed in the HBV group, with a mean ± SE of 11.01 ± 1.29, compared to 1.18 ± 0.12 in the control group ($p < 0.001$). As show in table (4) and figure (4).

Table 4: Comparison of mean of *miRNA185 gene expression* between patients and healthy controls.

Groups		***miRNA185 gene expression***
Chronic hepatitis B	Mean ± SE	11.01 ± 1.29
	Range	0.27-30.46
Control	Mean ± SE	1.18 ± 0.12
	Range	0.23-3.01
p-value		0.001** †

n: number of cases; †: Independent T test; **: significant at $P < 0.05$.

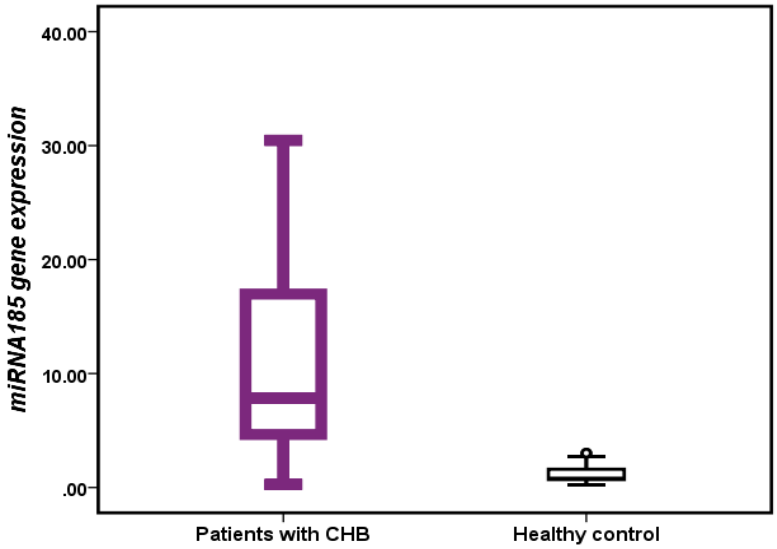

Figure 3-8: The means of *miRNA185 gene expression* in patients and control groups.

Diagnostic Accuracy of miRNA-185

Receiver operating characteristic (ROC) curve analysis was performed to assess the diagnostic accuracy of miRNA-185 in distinguishing chronic HBV patients from healthy controls. For miRNA-185, the analysis revealed an area under the curve (AUC) of 0.972 (95% CI: 0.925–1.000), with a sensitivity of 97.5%, specificity of 95.0%, positive predictive value (PPV) of 95.1%, and negative predictive value (NPV) of 97.4% at a cutoff value of >2.86-fold. As show in table (5) and figure (5)

Table (5): Sensitivity and specificity of *miRNA185 gene* (> 2.86-fold) in CHB.

miRNA185 gene	**patients *n* = 40**	**Healthy control *n* = 40**
> 2.86	39 (%)	2 (%)
< 2.86	1 (%)	38 (%)
Sensitivity %	97.5 %	
Specificity %	95.0 %	
PPV %	95.1 %	
NPV %	97.4%	
AUC (95% CI)	0.972 (0.925- 1.000)	

CI: Confidence interval, AUC: Area under curve.

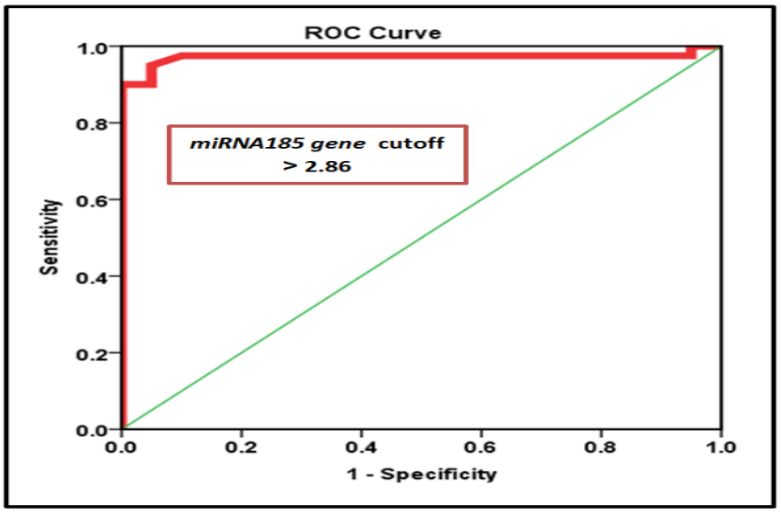

Figure (5): Receiver operator characteristic curve analysis of *miRNA185 gene* for the calculation of possible diagnostic cutoff value.

Relationship between miRNA Expression and Demographic/Lifestyle Factors

The analysis of miRNA-185 expression patterns across demographic and lifestyle factors in chronic HBV patients revealed no statistically significant associations with gender (male vs. female: miRNA-185 p = 0.878), smoking status (smoker vs. non-smoker: miRNA-185 p = 0.865), or alcohol consumption (drinker vs. non-drinker: miRNA-185 p = 0.552).

Correlation between miRNA Expression and Liver Function Tests

Correlation analyses between miRNA expression and liver function tests (ALP, GOT, GPT, and TSB) in chronic HBV patients showed no significant associations (all p > 0.05).

DISCUSSION

This work presents strong evidence for the efficacy of miRNA-185 as a dependable diagnostic biomarker for chronic HBV infection in Al-Diwaniyah City, Iraq. The results show that miRNA-185 is significantly overexpressed in chronic HBV patients compared to healthy controls, and it works very well as a diagnostic tool. The remarkable clinical accuracy of the MIRNA-185 is clear from AUC of 0.972, 97.5%sensitivity and uniqueness of 95.0%, indicates its ability to detect chronic HBV as highly reliable, non-invasive biomarks. It is better than standard liver function tests, which usually do not have the essential sensitivity and specificity of the first diagnosis and immunity.[3.4] Strong clinical abilities for MIRNA-185 are especially useful in places where complex clinical techniques are difficult to achieve, as they can help infected people find a reliable and easy way. It is believed that the complex interaction between the virus and the host's cellular machines causes the level of MIRNA-185 to grow with chronic HBV. It has been shown that the viral oncoprotein interacts with HBX and changes expression of different hosts Mirna, such as MIRNA-185.[17,18] This resolution of the host's MIRNA network is an important way that HBV can avoid immune responses and help itself survive and repeat.[19.20] Important transition of MIRNA-185 in chronic HBV patients is believed to be practical to facilitate the theft of the host-immunity surveillance virus and increase replication capacity. It turns out that the MIRNA-185 reduces the manifestation of the target and several host genes that are important for congenital and adaptable immune responses, such as those who are the code[23,24] for the interferon-electrated genes and antigen-produced molecules. By interrupting these essential immuneways, the MIRNA-185 can light the adaptation of HBV in the host.[25,26] In addition to helping HBV avoid the immune system, the MIRNA-185 has also been linked to controlling cellular activities that are important for the development of the disease, such as cell growth and death.[27,28] Excess manifestations of MIRNA-185 in individuals with chronic HBV can facilitate the progression of the complications of liver disease, such as cirrhosis and hepatosinoma (HCC), by increasing the existence and spread of infected hepatocytes, interru. The MIRNA-185 expression and the absence of remarkable relationship between demographic or lifestyle variables, including penis, smoking and alcohol intake, indicate that this MIRNA deformity is most affected by HBV infection instead of external factors.[31,32] This discovery confirms the dependence of MIRNA-185 as an independent biomarker, indicating that its clinical effect is not clearly affected by these misleading situations. The MIRNA-185 lacks sufficient associations between expression and standard liver function tests emphasizing various and autonomous mechanisms as it works in the context of MIRNA-cronic HBV infection.[5,6] It emphasizes its ability as a helpful clinical tool, as it may clarify aspects of HBV pathophysiology that is not indicated by traditional biochemical markers. The study indicates the remarkable clinical accuracy of MIRNA-185, as well as its mechanical significance in HBV-patogenesis, its ability as an auxiliary biomarker for chronic HBV infection. Starting it in clinical practice can facilitate initial diagnosis, better patient results and support the global

initiative to reduce the burden of liver disease related to HBV. The latter study should examine the possible medical use of targeting MIRNA-185 to chronic HBV infection. Because the MIRNA-185 is so important for viral replication and to avoid the immune system, changing the level or activity with medicines may be a new way of treating HBV.[33.34] In addition, in the prognosis of the emergence of HBV-related comoriding, including cirrhosis and HCC, which can increase its therapeutic projection[35.36], it is required to appear in the forecast to evaluate the future of MIRNA-185 to evaluate the future significance of the Mirna-185.

CONCLUSION

The current study provides compelling evidence for the use of miRNA-185 as a diagnostic biomarker for chronic HBV infection in Al-Diwaniyah City, Iraq. Its exceptional diagnostic performance, coupled with its mechanistic relevance in HBV pathogenesis, suggests that miRNA-185 could be a valuable tool for enhancing the early detection and management of chronic HBV infection.

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