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Assessment of Serum Glial Cell Line-Derived Neurotrophic Factor as a Diagnostic Marker for Patients with Liver Cirrhosis

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Abstract

Background: Cirrhosis is often irreversible and progressive phase of chronic liver disease recognized by loss of liver function and fibrotic remodeling. The aim of this study is to evaluate the diagnostic utility of glial cell line-derived neurotrophic factor (GDNF) in distinguishing cirrhosis patients from healthy individuals. Methods: A total of 61 participants were enrolled, consisting of 42 cirrhotic patients and 19 healthy controls. Serum GDNF, standard liver enzymes, kidney function parameters, and complete blood count indices were assessed. Results: Significant alterations were observed in liver profile markers such as decreased albumin and elevated bilirubin, aspartate aminotransferase (AST), gamma glutamyl transferase (GGT), and international normalized ration (INR) in cirrhotic patients ($P<0.001$). Hematological analysis revealed anemia, thrombocytopenia, and elevated red cell distribution width (RDW), along with increased neutrophil-to-lymphocyte ratio (NLR), indicative of systemic inflammation. GDNF levels were significantly elevated in cirrhosis cases, with a median of 2.3 ng/mL compared to 1.75 ng/mL in controls ($P=0.001$). GDNF demonstrated moderate diagnostic ability with an area under the ROC curve (AUC) of 0.699, sensitivity of 69%, and specificity of 73.7%, suggesting its potential as a non-invasive biomarker. RDW and NLR exhibited the highest diagnostic performance, with AUCs of 0.863 and 0.829, respectively. Conclusion: This result supports the integration of GDNF and other novel biomarkers to improve the early detection and clinical assessment of cirrhotic patients.

Keywords: Cirrhosis, Glial cell line derived neurotrophic factor (GDNF), Liver Enzymes.

Introduction

Liver cirrhosis is a chronic, progressive liver disease characterized by tissue-based development of renewing nodules bordered by fibrous strips as a result of persistent dysfunction of liver, leading to portal hypertension and end-stage liver dysfunction. It represents the advanced stage of fibrosis, where excessive extracellular matrix (ECM) deposition disrupts hepatic architecture, impairing liver function and blood flow. The

pathogenesis involves activation of hepatic stellate cells (HSCs), which transform into myofibroblasts under inflammatory certain conditions, leading to collagen deposition and sinusoidal capillarization, a process where liver sinusoidal endothelial cells lose their fenestrations, further exacerbating fibrosis. Portal hypertension, a major consequence of cirrhosis, arises from elevated intrahepatic vascular resistance and splanchnic vasodilation, contributing to adverse outcomes including ascites, variceal hemorrhage, and hepatic encephalopathy **(Xie and Benmassoud, 2025).**

Cirrhosis remains a significant public health burden, with an estimated 112 million cases, reflecting a rising prevalence compared to previous decades. The leading etiologies vary by area. HBV and HCV are prevalent in Asia and Africa, while NAFLD are common in Western countries. Notably, advancements in antiviral therapies for HBV and HCV have reduced viral-related cirrhosis, but metabolic and alcohol-related cases are increasing, partly due to rising obesity and alcohol consumption rates **(Wong and Huang, 2018).**

From clinical side, cirrhosis progresses from a compensated phase (often asymptomatic) to decompensation, marked by life-threatening problems. Common presentations include jaundice, ascites, coagulopathy, and hepatic encephalopathy, with diagnostic tools including liver biopsy and elastography. Management focuses on treating the underlying cause (antivirals for HBV/HCV, alcohol cessation), preventing complications such as diuretics for ascites and in advanced cases, liver transplantation **(Sterling et al.,2025).** Emerging evidence suggests that early fibrosis and even cirrhosis may be reversible with effective treatment, highlighting the importance of timely intervention. Despite therapeutic advances, cirrhosis remains a leading reason for mortality, accounting for 1.48 million deaths globally in 2019. Ongoing research into innovative therapeutic approaches and enhanced diagnostic tools offers hope for improving the care of individuals affected by cirrhosis **(Younossi et al.,2024).**

Patients and Methods:

Ethical Approval:

The Research and Ethical Committees of Al-Azhar Faculty of Medicine, Damietta, Egypt, approved this study IRB 00012367-2502-006.

Participants:

This study enrolled 61 participants, including 41 patients with cirrhosis and 19 healthy controls. Cirrhosis diagnosis was based on clinical, biochemical, and imaging findings.

Biochemical Analysis:

Serum samples were collected from all participants one day prior to any surgical intervention (where applicable). The following biochemical parameters were measured using standardized assays and methods at the Gastroenterology Surgery Center, Mansoura, Egypt: aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP), albumin, total bilirubin (Tbili), direct bilirubin (Dbili), gamma-glutamyl transferase (GGT), international normalized ratio (INR), red blood cell (RBC) indices, white blood cell (WBC) indices and platelet indices. Serum GDNF levels were also determined using a validated assay.

Statistical Analysis:

SPSS statistics software version 26.0 (Statistical package for social science Inc., Chicago, IL, USA) was used to perform the statistical analysis. Continuous variables were expressed as mean ± standard deviation for normally distributed data or median (interquartile range) for non-normally distributed data. Differences in continuous variables between the control and cirrhosis groups were assessed using an independent samples t-test for normally distributed data or a Mann-Whitney U test for non-normally distributed data. The diagnostic accuracy of GDNF and other relevant indices in distinguishing cirrhosis patients from healthy controls was assessed by calculating the area under the Receiver Operating Characteristic (ROC) curve (AUC), sensitivity, and specificity. Statistical significance was set at $p < 0.05$.

Results:

Clinical features of cirrhosis and control

group.

Median age of the control group was 26 years (IQR: 24–34), while the cirrhosis group had a significantly higher median age of 51 years (IQR: 34–60) with a p-value of 0.001. The gender distribution was similar between the groups. In the control cohort, 73.7% of the participant were male and 73.8% of the cirrhosis patients (P=0.978). HBsAg positivity was observed in 7.1% of the cirrhosis group, while none of the controls were positive. HCVAb positivity was markedly higher in the cirrhosis group (61.9%) versus controls (0%), with a P-value of 0.001.

Regarding liver disease severity, Child-Pugh classification showed that 41% of the cirrhosis group were classified as Child C, while all control subjects were classified as Child A. APRI scores revealed that 50% of the cirrhosis group had a score of 3, compared to none in the control group (P=0.001). FIB-4 scores were also significantly different (P=0.001), with 60% of cirrhosis patients scoring 3, whereas all individuals in the control group had a score of 1. These findings summarize the distribution of key clinical parameters among the study groups (Table.1).

Table (1) Clinical characteristics of cirrhosis and control group.

Variable Median (IQR)	Control Group N=19	Cirrhosis group N=42	P-value
Age (yr)	26 (24-34)	51 (34-60)	0.001
Gender			
Male n (%)	14 (73.7)	31 (73.8)	0.978
Female n (%)	5 (26.3)	11 (26.2)	
HBsAg n (%)			
+ve	0 (0)	3 (7.1)	0.603
-ve	19 (100)	38 (90.5)	
HCVAb n (%)			
+ve	0 (0)	3 (7.1)	0.001
-ve	19 (100)	26 (61.9)	
Child n (%)			
A	19 (100)	7 (17.9)	0.001
B	0 (0)	16 (41)	
C	0 (0)	16 (41)	
APRI n (%)			
1	18 (94.7)	7 (19.4)	0.001
2	1 (5.3)	11 (30.6)	
3	0 (0)	18 (50)	
FIB4 n (%)			
1	19 (100)	4 (11.4)	0.001
2	0 (0)	10 (28.6)	
3	0 (0)	21 (60)	

HBsAg - Hepatitis B surface antigen, HCVAb - Hepatitis C virus antibody, Child - Child-Pugh score, APRI - Aspartate Aminotransferase to Platelet Ratio Index, FiB4 - Fibrosis-4 Index.

Serum level of glial cell line derived neurotrophic factor for cirrhosis and the control group.

Median GDNF levels were significantly higher in the cirrhosis group (2.3 ng/ml, $P = 0.019$) compared to the control group (1.75 ng/ml).

Table (2) Serum level of glial cell line derived neurotrophic factor for cirrhosis and control group.

Variable Median (IQR)	Control Group N= (19)	Cirrhosis group N= (42)	P value
GDNF (ng/ml)	1.75 (1.20 – 2.04)	2.3(1.6- 2.)	0.001

GDNF - Glial Cell Line-Derived Neurotrophic Factor.

Serum levels of kidney profile for the studied groups.

The median serum creatinine level was 0.80 mg/dL (IQR 0.70-0.90) in the control group and 0.70 mg/dL (IQR 0.60-0.90) in the cirrhosis group, with a P-value of 0.693. The mean serum potassium level was 4.30 ± 0.449 mmol/L in the control group and 4.04 ± 0.60 mmol/L in the cirrhosis group, yielding a P-value of 0.332. For uric acid, the mean serum level was 5.02 ± 1.93 mg/dL in the control group and 4.75 ± 1.75 mg/dL in the cirrhosis group, with a corresponding p-value of 0.509. These results indicate that there were no statistically significant differences in the serum levels of creatinine, potassium, and uric acid between the control and cirrhosis groups (Table.3).

Table (3) Serum levels of kidney profile for the studied groups.

Variables	control group N= (19)	Cirrhosis group N= (42)	P - Value
Cr(mg/dL) Median (IQR)	0.80 (.70-.90)	0.70 (0.60-0.90)	0.693
K(mmol/l) Mean ± SD	4.30±.449	4.04±.60	0.332
UA (mg/dL) Mean ± SD	5.02±.93	4.75±1.75	0.509

Cr – Creatinine, K – Potassium, UA - Uric Acid

Serum levels of different liver profile for the studied groups.

The serum levels of different liver function parameters in the control group (N=19)

and the cirrhosis group (N=42). Levels of serum albumin were significantly lower in the cirrhosis group (median 3.3 g/dL, IQR 2.70–3.77) versus the control group (median 4.50 g/dL, IQR 4.40–4.80), with a p-value of <0.001. Total bilirubin and direct bilirubin levels were also significantly higher in cirrhosis patients, with medians of 1.6 mg/dL and 1 mg/dL, respectively, compared to 0.60 mg/dL and 0.15 mg/dL in controls (P<0.001for both). Liver enzymes showed marked differences between the groups. ALP was higher in the cirrhosis group (median 65 U/L) than in controls (median 5 U/L), while AST was also increased in the cirrhosis group (median 41.5 U/L) compared to controls (median 21 U/L), with both showing statistical significance (P<0.001). ALT levels were higher in cirrhotic patients than in controls (P<0.001). GGT was notably elevated in cirrhosis patients (median 46 U/L) compared to the control group (median 17 U/L), and INR was higher in cirrhosis (median 1.4) than in controls (median 1.0), both with P-values <0.001(Table.4).

Table (4) Serum levels of different liver profile for the studied groups.

Variables Median (IQR)	Control Group N= (19)	Cirrhosis group N= (42)	P - Value
Alb(g/dL)	4.50 (4.40 – 4.80)	3.3 (2.70-3.77)	<0.001
T.bili(mg/dL)	0.60 (.50- .70)	1.6(1-4.6)	<0.001
D.bili(mg/dL)	0.15 (0.10- 0.25)	1(.47-2.4)	<0.001
ALP(U/L)	5(5-5)	6(5-7)	<0.001
AST(U/L)	21 (20 – 21)	41.5 (26.7-72.2)	<0.001
ALT(U/L)	23 (21 – 27)	27.5 (21-44.5)	<0.001
GGT(U/L)	17 (12 – 27)	46(30-94)	<0.001
INR	1 (1 – 1.10)	1.4(1.2-1.6)	<0.001

Alb – Albumin, T.bili - Total Bilirubin, D.bili - Direct Bilirubin, ALP - Alkaline Phosphatase, AST - Aspartate Aminotransferase, ALT - Alanine Aminotransferase, GGT - Gamma-Glutamyl Transferase, INR - International Normalized Ratio.

Red blood cells and their indices for the studied groups.

Red blood cells and their indices for the control group (n=19) and the cirrhosis group (n=42). The table displays median values with interquartile ranges (IQR) for red blood cell count (RBCs), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), and red cell distribution width (RDW). Additionally, mean values with standard deviations (SD) are provided for hemoglobin (HG) and hematocrit (HCT). An overall P-value is included for each variable to indicate the statistical significance of the difference between the two categories. The results demonstrate markedly significant differences (P<0.001) between the control and cirrhosis groups for RBCs (3.8 x 10^6/cell/µL, IQR 3.1-4.2 vs. 5.20 x 10^6/cell/µL, IQR 4.60-5.40), HG (10.5 ± 2.2 g/dL vs. 14.26 ± 1.51 g/dL), HCT (31.4 ± 6.7 % vs. 41.79 ± 5.38 %), and RDW (15.1 %, IQR 13.1-16.9 versus 12.30 %, IQR 11.50-13.05). In contrast, no statistically significant differences were found in MCV (P=0.099), MCH (p=0.094), and MCHC (P=0.529) between the two groups (Table.5).

Table (5) Red blood cells and their indices for the studied groups.

Variable	Control group N= (19)	Cirrhosis group N= (42)	P - Value
RBCs×10^6(Cell/µL) Median (IQR)	5.20 (4.60 – 5.40)	3.8 (3.1-4.2)	<0.001
HG (g/dL) Mean ± SD	14.26 ± 1.51	10.5±2.2	<0.001
HCT (%) Mean ± SD	41.79±5.38	31.4±6.7	<0.001
MCV (fL) Median (IQR)	82.46(80.16 – 86.20)	87 (80.4-90.9)	0.099
MCH (pg) Median (IQR)	28.50 (27.8 – 29.25)	29.2 (26.5-31.8)	0.094
MCHC(g/dL) Mean ± SD	34.30±1.72	33.38±3.03	0.529
RDW (%) Median (IQR)	12.30(11.50 – 13.05)	15.1 (13.1-16.9)	<0.001

RBCs - Blood Cell Count, HG – Hemoglobin, HCT – Hematocrit, MCV - Mean Corpuscular Volume, MCH - Mean Corpuscular Hemoglobin, MCH - Mean Corpuscular Hemoglobin, MCHC - Mean Corpuscular Hemoglobin Concentration, RDW - Red Cell Distribution Width.

Platelets and their indices for the studied groups:

The cirrhosis group demonstrated significantly lower platelet count (P=0.002) and Pct (<0.001), along with a significantly higher platelet distribution width (P=0.040) and PLCR (P=0.011) versus the controls. No statistically significant differences were found in MPV (P=0.115) and PLR ratio (P=0.942) between the

two categories (Table.6).

Table (6) Platelets and their indices for the studied groups.

Variable	Control group N= (19)	Cirrhosis group N= (42)	P - Value
PLT×10^3 (cell/µL Median (IQR)	209(191.9 – 252.9)	89.3(55-148.8)	0.002
PDW (fL) Median (IQR)	13(11.60 – 10.20)	17.9(12.6-20.1	0.170
MPV (fL) Median (IQR)	9.30(6.50 – 10.50)	10.5(7.4-11.3)	0.115
Pct (%) Median (IQR)	0.194(.126-.206)	0.08(.05-.16)	<0.001
PLCR (%) Mean±SD	27.1±6.7	35.8±8.03	0.011
PLR Median (IQR)	83.6(71.22 – 112.22)	91.4(57.7-135)	0.942

PLT - Platelet Count, PDW - Platelet Distribution Width, MPV - Mean Platelet Volume, Pct - Plateletcrit (percentage of blood volume occupied by platelets), PLCR - Platelet Large Cell Ratio, PLR - Platelet-to-Lymphocyte Ratio.

White blood cells and their indices for the studied groups

White blood cells and their indices for the control group (n=19) and the cirrhosis group (n=42). The cirrhosis group showed a significantly lower WBC count (P=0.006) and absolute lymphocyte count (P<0.001), along with a significantly higher neutrophil percentage (P<0.001) and NLR (P<0.001) relative to the controls. The lymphocyte percentage was significantly lower in the cirrhosis group (P<0.001). No statistically significant difference was observed for the absolute neutrophil count shared by the two categories (P=0.699) (Table.7).

Table (7) White blood cells and their indices for the studied groups.

Variable	Control group N= (19)	Cirrhosis group N= (42)	P – Value
WBC×10^3 (cell/µL) Median (IQR)	5.7 (4.2-6.9)	4(2.9-5)	0.006
Lymph No×10^3 (cell/µl) (Median (IQR)	2.50 (1.90- 3.05)	0.85(0.67-1.5)	<0.001
Neut No×10^3 (cell/µl) Median (IQR)	2.16(1.70 – 3.10)	2.10(1.5-3.2)	0.099
Lymph% Mean ± SD	43.7±7.5	27.16±12.4	<0.001
Neut % Mean ± SD	43.7±8.4	57.7±14.4	<0.001
NLR Median (IQR)	0.96(0.80-1.22)	2.3(1.3-3.6)	<0.001

WBC - White Blood Cell Count, Lymph no - Lymphocyte Number, Neut no - Neutrophil Number, Lymph % - Lymphocyte Percentage, Neut % - Neutrophil Percentage, NLR - Neutrophil-to-Lymphocyte Ratio.

Area under curve (AUC), sensitivity, and specificity of some variables for Diagnosis of patients with cirrhosis versus control group.

The diagnostic performance of several biomarkers for distinguishing patients with cirrhosis from the control group, among these, RDW (AUC: 0.863, P < 0.001) and NLR (AUC: 0.829, P < 0.001) demonstrated the highest accuracy, combining strong sensitivity (81% and 82%, respectively) and specificity (78% and 73%, respectively). PLCR also performed well (AUC: 0.809, *P* = 0.006), with the highest sensitivity (84%) but moderate specificity (63%). GDNF achieving an AUC of 0.699 and balanced sensitivity (69%) and specificity (73.7%). Plateletcrit (Pct) provided good sensitivity (82%) with specificity of (56%), and an AUC of 0.789 (*P* < 0.001) (Table.8) (Fig.1 .2.3.4 and 5).

Table (8) Area under curve (AUC), sensitivity, and specificity of some variables for Diagnosis of patients with cirrhosis versus control group.

Variable	AUC	Cutoff	Sen%	Spe%	95% CI	P value
GDNF (ng/ml)	0.699	2.2	69%	73.7%	0.558-0.841	.0.013
NLR	0.829	1.1	82%	73%	0.724-0.933	<0.001
RDW (%)	0.863	13	81%	78%	0.768-0.958	<0.001
PLCR (%)	0.809	30	84%	63%	0.646-0.971	0.006
Pct (%)	0.789	0.18	82%	56%	0.670-0.909	<0.001

GDNF - Glial Cell Line-Derived Neurotrophic Factor, NLR - Neutrophil-to-Lymphocyte Ratio, RDW - Red Cell Distribution Width, PLCR - Platelet Large Cell Ratio, Pct - Plateletcrit (percentage of blood volume occupied by platelets).

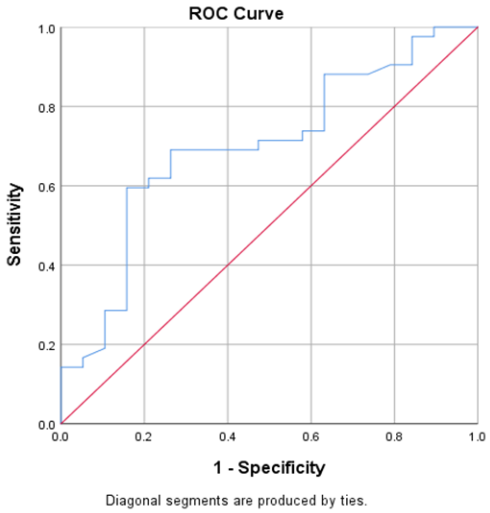

Figure (1): ROC curve of GDNF for Cirrhosis patients versus control group

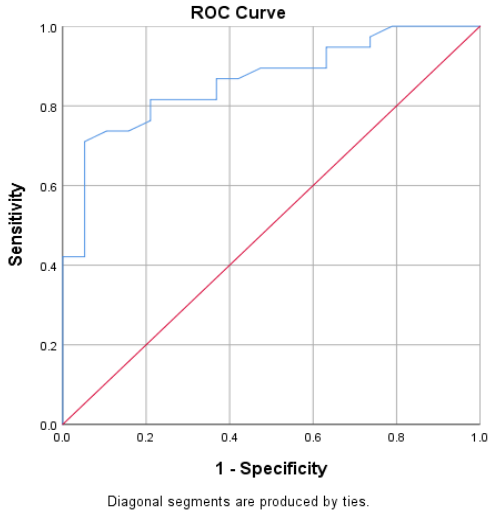

Figure (2): ROC curve of RDW for Cirrhosis patients versus control group

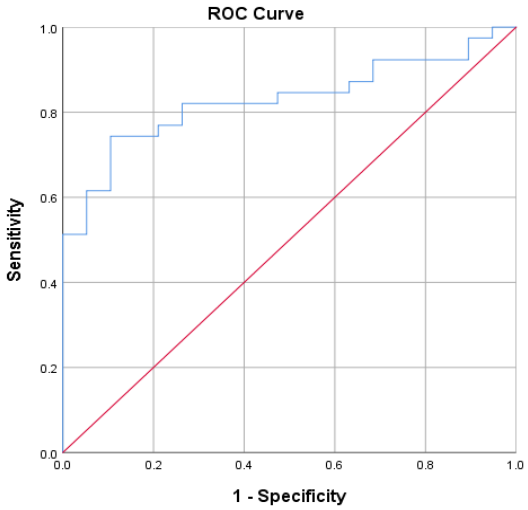

Figure (3): ROC curve of NLR for Cirrhosis patients versus control group

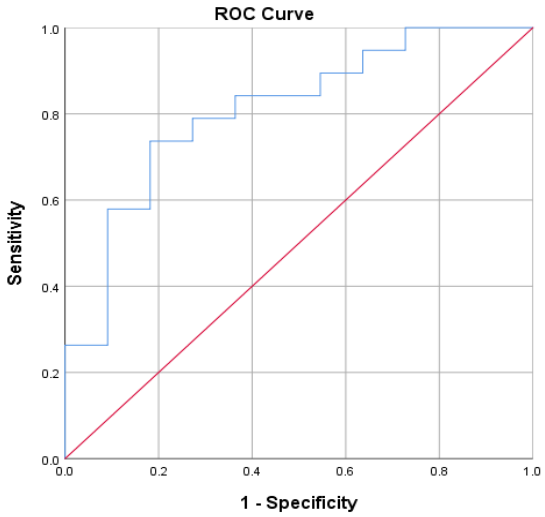

Figure (4): ROC curve of PLCR for Cirrhosis patients versus control group

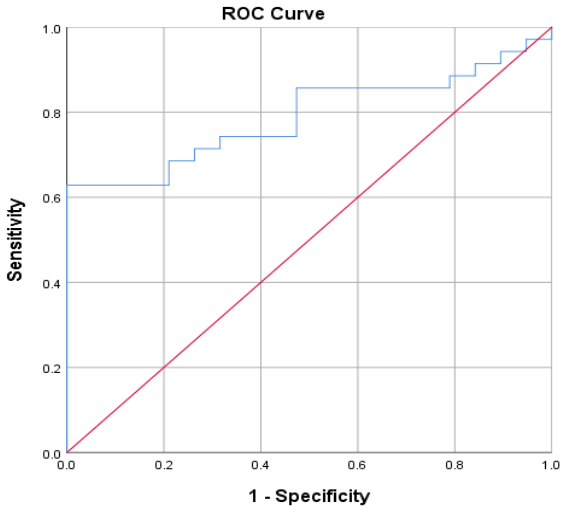

Figure (5): ROC curve of Pct for Cirrhosis patients versus control group

Discussion:

Cirrhosis, the culmination of different liver injuries, originates from a process of necroinflammation followed by fibrogenesis. Histologically, it is defined by widespread nodular regeneration encased within thick fibrous bands, ultimately resulting in the loss of functional liver tissue and the breakdown of its structural framework (**Pampin et al., 2018**). This architectural disruption significantly impedes portal blood flow, leading to both portal hypertension and impaired hepatic synthetic function. Historically viewed as a terminal condition inevitably resulting in

mortality without liver transplantation. Cirrhosis is treatable but not curable. There are two targets when treating this illness, the first is to prevent the destruction of the liver while the second is to stop the complications **(Zhou et al., 2014).**

The significantly increased serum GDNF levels found in the cirrhosis group (2-3 ng/ml, IQR 1.6-2.0) versus the controls (1-7 ng/ml, 1-20-2-04) (P=0.001) demonstrate a potential role of this marker in the context of liver cirrhosis. The chronic liver injury, fibrogenesis and inflammation may trigger an upregulation of GDNF production. Previous studies have suggested that GDNF can be expressed by several cell types within the liver, including hepatocytes and hepatic stellate cells (HSC) **(Wang et al., 2018**). Activated HSC have been shown to produce GDNF, and GDNF itself has been implicated in promoting HSC proliferation and activation. likely contributing to the progression of fibrosis **(Wang et al., 2018).** The observed elevation of circulating GDNF in cirrhosis patients might reflect a systemic response to the ongoing liver damage **(Zhang et al., 2021).**

One outcome from this study does not indicate major alterations in levels of potassium. Previous studies indicate that cirrhosis cases, particularly those on diuretics or with ascites, are prone to hypokalemia because of renal potassium wasting **(Huang et al., 2021; Gurnani et al., 2021).** In the context of uric acid, its levels were not significantly different in the studied groups. Previous studies suggested a possible correlation between elevated uric acid levels, increased oxidative stress and inflammation in cirrhosis cases, suggesting that uric acid is potentially implicated in the progression of liver disease. The uric acid levels are often elevated in metabolic disorders correlated with liver dysfunction, like cirrhosis and NAFLD **(Sirota et al., 2013; Yang et al, 2022).**

Results of serum liver profile indicated significant biochemical derangements in cirrhotic patients versus controls, The significantly decreased albumin levels in the cirrhotic patients (P<0.001) align with the compromised synthetic function of the cirrhotic liver, a hallmark of the disease. Reduced albumin levels in patients with CLD may signal the onset of cirrhosis. A decline in plasma albumin is associated with cirrhosis, as these patients exhibit impaired albumin production and compromised liver cell function. In advanced phases of cirrhosis, albumin levels can decrease by as much as 60–80% **(Carvalho and Machado,2018).** Increased total and direct bilirubin (P<0.001) are well-established characteristic of cirrhosis, hyperbilirubinemia works as an t indicator of impaired liver function and often linked to the jaundice observed in cirrhotic patients **(Lee et al.,2020).**

Elevated ALP, AST, and GGT in the cirrhosis group (P<0.001) are key indicators of cholestasis and hepatocellular injury. AST, a transaminase enzyme found in hepatocytes, is released into bloodstream upon liver cell damage its increased levels serve as a marker of hepatocellular damage **(Lai et al., 2024)**. GGT is usually increased in different liver diseases, including cirrhosis, and can be sensitive to cholestasis and alcohol-related liver injury (Giannini et al., 2005). Levels of ALT (P < 0.001) is often normal or mildly increased in advanced stages of cirrhosis, as the liver has limited functioning tissue left to release enzymes **(Trapper and Lok, 2017).**

Regarding RBC Indices, the cirrhosis patients demonstrated significantly Lower RBCs, HGB and HCT (P<0.001), indicating the presence of anemia, a well-known outcome of chronic liver disease usually resulting from blood loss, hypersplenism and impaired erythropoietin Production **(Xie et al., 2016)**. RDW was significantly higher in cirrhotic patients' group (<0,001), reflecting increased Variation in red blood cells size.

This study demonstrated significant alteration in white blood cell and platelet indices. Patients with cirrhosis exhibited reduced total white blood cell and lymphocyte counts, accompanied by an elevated neutrophil percentage and NLR ratio, indicating systemic inflammation. Furthermore, NLR commonly identified as a useful biomarker for assessing prognosis in patients with cirrhosis (**Peng et al., 2018; Wang et al., 2012)**. They also had significantly lower platelet counts and Pct, but higher PDW and PLCR, suggesting thrombocytopenia with altered platelet characteristics. These hematological alterations are consistent with the immune dysregulation and bone marrow suppression often associated with chronic liver disease **(Peng et al., 2018).**

The diagnostic evaluation of different biomarkers for distinguishing cirrhosis patients from control group reveals insightful differences in their performance metrics,

particularly sensitivity, specificity, and area under the curve (AUC). Among the studied parameters, GDNF achieved a moderate AUC of 0.699, with relatively balanced sensitivity (69%) and specificity (73.7%), indicating its potential as a supplementary marker. A study carried out by **Yang et al. (2022)** which employed both ELISA- based serum analysis and histological liver biopsy demonstrated the GDNF levels were significantly increased in liver fibrosis and cirrhotic patients, suggesting its role as non-invasive diagnostic biomarker. Furthermore, GDNF demonstrated good diagnostic value in identifying cirrhotic patients from healthy controls, with reported AUC of 0.84. This performance surpasses classical fibrosis indices such as APRI score, FIB-4 index, specifically in differentiating advanced fibrosis. The optimal cutoff for GDNF in predicting cirrhosis was 33.8 pg/mL, with significantly higher levels observed in cirrhotic patients compared to those without cirrhosis (33.8 versus 23.5 pg/mL, $P < 0.001$). These results suggest that GDNF may serve as a non-invasive diagnostic marker for cirrhosis.

For diagnosis of cirrhotic patients versus controls, RDW exhibited the most promising diagnostic potential with an AUC of 0.863 $P < 0.001$), high sensitivity of 81%, and specificity of 78%, suggesting robust discriminative power. Similarly, NLR demonstrated comparable accuracy, with an AUC of 0.829 ($P < 0.001$), sensitivity of 82%, and specificity of 73%, demonstrating its usefulness as a non-invasive inflammatory marker in liver pathology **(Zhao et al., 2019).** NLR exhibited comparable accuracy, with an AUC of 0.829 ($P < 0.001$), sensitivity of 82%, and specificity of 73%, showing its value as a non-invasive inflammatory marker in liver pathology **(Zhao et al., 2019).** PLCR also showed favorable diagnostic ability, achieving high sensitivity (84%), although its specificity was moderate at 63%, with an AUC of 0.809 ($P = 0.006$). Previous literature reported that PLCR level was significantly higher in cirrhotic patients and correlated with disease severity, proposing its possible role as non-invasive marker for liver fibrosis progression **(Zanetto, 2023).** Pct achieved an AUC of (0.789 $P < 0.001$), sensitivity of 82%, and specificity of 56%, suggesting moderate diagnostic utility **(Michalak et al., 2021).** Overall, these findings underscore the role of combining multiple biomarkers, particularly those introducing hematological and inflammatory changes, to facilitate early diagnosis and monitoring of liver cirrhosis.

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الملخص العربي

عنوان البحث: تقييم العامل العصبي المغذي المشتق من الخلايا الدبقية في المصل كدلالة تشخيصية لمرضى تليف الكبد

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الخلفية: غالباً ما يكون تليف الكبد مرحلة غير قابلة للتراجع ومتقدمة من أمراض الكبد المزمن، تتميز بفقدان وظائف الكبد وإعادة التشكيل التليفي. الهدف: تهدف هذه الدراسة إلى تقييم الفائدة التشخيصية للعامل العصبي المغذي المشتق من الخلايا الدبقية (GDNF) في التمييز بين مرضى التليف الكبدي والأفراد الأصحاء. الطرق: تم إشراك ما مجموعه ٦١ مشاركاً، منهم ٤٢ مريضاً بتليف الكبد و١٩ شخصاً سليماً كضوابط. تم تقييم مستوى GDNF في المصل، وإنزيمات الكبد التقليدية، ومعايير وظائف الكلى، ومؤشرات تعداد الدم الكامل. النتائج: لوحظت تغيرات كبيرة في مؤشرات ملف الكبد مثل انخفاض الألبومين وارتفاع البيليروبين، وأنزيم أسبارتات أمينوترانسفيراز (AST)، وغاما جلوتاميل ترانسفيراز (GGT)، والنسبة المعيارية الدولية (INR) لدى مرضى التليف الكبدي (P<0.001). كشف التحليل الدموي عن فقر الدم، ونقص الصفيحات الدموية، وارتفاع عرض توزيع كريات الدم الحمراء (RDW)، بالإضافة إلى ارتفاع نسبة العدلات إلى اللمفاويات (NLR)، مما يشير إلى التهاب جهازي. كانت مستويات GDNF مرتفعة بشكل ملحوظ في حالات التليف الكبدي، بمتوسط ٢,٣ نانوجرام/مل مقارنة بـ ١,٧٥ نانوجرام/مل في الضوابط (P<0.001). أظهر GDNF دقة تشخيصية متوسطة بمساحة تحت منحنى خصائص التشغيل المستقبلة (AUC) بلغت ٠,٦٩٩، وحساسية ٦٩%، وخصوصية٧٣,٧%، مما يشير إلى قدرته كعلامة حيوية غير جراحية. أظهر مؤشرا RDW وNLR أعلى أداء تشخيصي، بقيم AUC بلغت ٠,٨٦٣ و٠,٨٢٩ على التوالي. الاستنتاج: تدعم هذه النتيجة دمج GDNF والمؤشرات الحيوية الجديدة الأخرى لتحسين التشخيص المبكر والتقييم السريري لتليف الكبد.