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Original article

Diagnostic Value of Adiponectin in Assessment of Liver Fibrosis in Children with Chronic Liver Diseases

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Abstract:

Background: A long-standing, irreversible alteration in the hepatic structure is implied by the term chronic liver diseases (CLD), which may result in complications such as cirrhosis and premature mortality. The present research aimed to examine the significance of serum Adiponectin in the assessment of liver fibrosis in CLDs in children. **Methods:** This case-control study included fifty children with CLDs (CLD group) of different etiologies and fifty healthy children, age, and sex matches as a control group. All participants underwent a comprehensive medical history review, full clinical examination, and laboratory investigations. Serum Adiponectin was assessed using Human Adiponectin ELISA kit. **Results:** CLD group had statistically significant higher adiponectin compared to control group. Adiponectin was statistically significant higher in children with higher degrees of fibrosis and HAI score compared to children's lower degrees. Adiponectin had a statistically significant positive correlation with (total and direct bilirubin, AST, ALT, ALP, GGT, PT, PTT, INR, APRI score, FIB-4, Child-Pugh, PELD and MELD) and statistically negative correlation with (hemoglobin, platelets, albumin). At a cutoff point > 12.5 µg/mL, adiponectin could predict mild to moderate fibrosis with sensitivity 94% and specificity 98%. At a cutoff point > 29.4 µg/mL, it could detect cases with severe fibrosis with sensitivity 91% and specificity 89.9%. **Conclusion:** Liver fibrosis severity in children with CLDs may be identified by adiponectin, a conceivable noninvasive biochemical marker.

Keywords: Adiponectin; Liver Fibros; Children; CLD

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Introduction

Chronic liver disease (CLD) can progress to end-stage liver disease (ESLD) in the absence of treatment [(1)].

Metabolic, autoimmune, and infectious factors comprise the etiological spectrum of CLD in children. The diagnosis may be incidental, meaning it is made as part of a workup of symptoms that are either unrelated or indirectly related, or it may be made becaemploy of the children exhibiting a variety of hepatic presentations, often in the later phases of the disease. Therefore, it is imperative to provide prompt diagnosis and treatment prior to the patient's progression to ESLD in order to reduce morbidity and mortality [(2)].

As exhibited, investigative reports and clinical expertise allow for a more precise etiological diagnosis of CLD in pediatric populations. However, liver biopsy (LB) remains the preferred method for determining the etiology in most of these patients, provided cirrhosis is not present. Nevertheless, the pediatric population frequently encounters challenges in obtaining consent from primary caregivers for LB, which is notoriously invasive. Complicating matters is another risk that comes with LB [(3)].

Chronic renal disease, type 2 diabetes mellitus and pregnancy-related metabolic alterations are among the numerous inflammatory conditions that are associated with adipokines. One important adipokine, adiponectin, has been associated with the inflammation that follows obesity and metabolic syndrome [(4)].

In particular, adipose tissue is the primary source of adiponectin, an adipokine [(5)], exerts pleiotropic effects on various metabolic pathways and has been linked to the modulation of inflammation, oxidative stress, and insulin resistance [(6)].

This research examined serum adiponectin titers as a potential indicator of liver fibrosis in pediatric patients with CLD.

Patients and methods

This case-control study involved fifty children diagnosed with CLD (CLD group) of varying etiologies, referred from the pediatric hepatology unit at Benha University Hospitals, and fifty age- and sex-matched healthy children serving as the control group. The study period is from May 2021 to May 2025

Inclusion Criteria:

All participants were children under the age of eighteen who had been diagnosed with CLDs of different etiologies (including HBV, HCV, autoimmune, and metabolic liver diseases). Diagnosis was confirmed through clinical examinations, laboratory investigations, and LB.

Exclusion Criteria:

Children with CLDs complicated by comorbidities such as cardiac, renal, or malignancy were excluded from the study.

A thorough clinical examination, complete blood count (CBC), liver function tests (including AST, ALT, GGT, alkaline phosphatase, serum albumin, total bilirubin [TB], and direct bilirubin [DB]), coagulation profile (PT, PTT, INR), and serum Adiponectin levels were performed for all participants.

- **Blood Sample Collection:**

Venous blood samples were drawn under strict aseptic conditions:

- One milliliter of whole blood was collected in an EDTA vacutainer and gently mixed, to be employed for the CBC.
- Two milliliters of blood were placed into a 3.2% sodium citrate vacutainer for coagulation function tests, including activated partial thromboplastin time (APTT) and international normalized ratio (INR).
- Five milliliters of blood were drawn into a plain test tube and allowed to coagulate. After coagulation, the samples were centrifuged at 1,500 rpm for 15 minutes, and the separated serum was employed for the liver function tests, including ALT, AST, albumin, bilirubin (TB and DB), GGT, and alkaline phosphatase.

Additionally, 1 milliliter of serum was stored at -20°C for later assay of Adiponectin.

- CBC was analyzed for all samples using the XS Series automated hematology analyzer (SN 12526, SYSMEX Corporation, Kobe, Japan).
- Biochemical liver function tests were conducted by DIALAB (13771103, Thermo Company, USA).
- Coagulation Function (APT and INR): using Automated blood coagulation analyzer CS-1600, SN 12058, Sysmex Corporation, Kobe, Japan.
- Serum Adiponectin level was assessed using Human Adiponectin ELISA kit. CUSABIO TECHNOLOGY LLC (CUBIO Innovation Center), Houston, TX 77054, USA. (Catalog Number. CSB-E07270h), By TECAN Infinite F50 ELISA reader, Singapore, S.N. 1306007553

Abdominal ultrasonography was done for all patients to assess liver size and spleen size and presence of Ascites. Using a modified Menghini aspiration instrument, LB was performed on all patients. At least 10-12 portal tracts should be present in an adequate core. Following the fixation of the excision specimen in 10% formalin, it was embedded in paraffin. Using a modified Ishak scoring system, the histological activity of hepatitis was evaluated. The five micrometer thick sections were stained on a glass slide using hematoxylin and eosin [(7)].

The Histological Activity Index (HAI) and fibrosis staging are essential tools employed to evaluate LB samples, providing insight into the severity of liver disease. The HAI score, which ranges from 0 to 18, assesses the level of liver activity, with scores categorized as minimal (1–3), mild (4–8), moderate (9–12), and severe (13–18). These scores reflect the degree of inflammation and cellular injury present in the liver tissue. Similarly, the fibrosis score classifies the extent of fibrosis in the liver, starting from a score of 0, which indicates no fibrosis, and progressing through various stages. Stage 1 reflects fibrous expansion of some portal areas, with or without short fibrous septa, while stage 2 shows fibrous expansion of most portal areas. Stage 3 represents fibrous expansion of most portal areas with occasional portal-to-portal bridging. Stage 4 involves marked fibrous expansion with bridging, both portal-to-portal and portal-to-central. Stages 5 and 6 indicate advanced fibrosis, with incomplete cirrhosis marked by occasional nodules in stage 5, and cirrhosis, either probable or definite, in stage 6 [(7)].

Ethical considerations

The whole study design was approved by the local ethics committee, Faculty of Medicine, Benha University (Approval number; MS 14-4-2024). Confidentiality and personal privacy were upheld at every stage of the investigation. At any time, guardians were permitted to disengage from the study without incurring any repercussions. None of the data that was collected was or will be utilized for any other purpose.

Approval code: MS 18-4-2024

Statistical analysis

For data tabulation and analysis, we utilized SPSS, Inc.'s (Chicago, IL, USA) version 16 software. We employed the Shapiro-Wilk test to make sure the data was normal. The mean and standard deviation (± SD) label parametric numerical data, whereas the median and interquartile range (IQR) denote non-parametric numerical data.

Statistics that are not numerical in nature, including frequency and %. We compared the meanings of the two groups to look for a statistically significant difference. We employed the Student T Test for this analysis. The one-way ANOVA could compare the means of two or more groups. It was my expectation that the Mann Whitney U test for non-parametric variables would reveal a noteworthy distinction between the two sets of data. To examine the categorical data, X^2 and Fisher’s Exact Test (FET) were utilized.

The existence of a relationship between non-parametric variables was confirmed by the computed Spearman's correlation coefficient (rho). The researchers in this study exhibited the optimal cutoff values for the indicators by using ROC curve analysis, which maximizes specificity and sensitivity. In the study, a p-value was considered significant if it was less than the predefined level of 0.05.

Results

This study included fifty children with CLD group and fifty healthy children, age, and sex matches as a control group. CLD group included 27 females (54%) and 23 males (46%), their mean age was 9.1±3.7 years, 48% of cases had history of positive consanguinity, 24% had family history of liver diseases. CLD group had statistically significant higher frequency of positive family history of liver diseases compared to control group. While there was insignificant difference between groups as regards to age, sex, or consanguinity.

The mean disease duration was 7.41.9 years, the mean age at disease beginning was 3.11.7 years, and glycogen storage disease was the most prevalent caemploy of liver disease (40%), followed by autoimmune hepatitis (28%). Abdominal distension (30%), gastric pain (24%), convulsions (18%), jaundice (16%), anorexia (12%), and exhaustion (12%) were the most prevalent initial symptoms (Table 1).

Comparing the CLD group to the control group, we find that their AST, ALT, ALP, GGT, TB, DB, PT, PTT, and INR are all significantly higher, while their hemoglobin and platelet counts are much lower. Groups did not differ significantly with respect to white blood cells, serum albumin (Table 2).

The mean APRI score was 2.7±1.9 and the mean FIB-4 score was 10.6±2.7., the mean Child Pugh score was 7.2±1.7, the mean PELD was 8.5±2.9, the mean MELD was 8.2±2.1,

LB results in the studied group according to Ishak score exhibited that most cases (42%) had mild fibrosis, while 20% had moderate fibrosis and 16% had mild-moderate fibrosis. Regarding HAI, 42% of patients were minimal, 34% of patients were mild, and 12% were moderate and 12% were severe. Most cases had mononuclear inflammatory cells (48%), 32% had lymphocytes infiltrates (Table 3).

CLD group had statistically significant higher adiponectin (median: 21.6, IQR: 19.6-24.2 μg/mL) compared to control group (median: 5, IQR: 4.3-6.1 μg/mL), $p<0.001$ (figure 1). Adiponectin was statistically significant higher in children with higher degree of fibrosis (median was 19.2 in F0, 21.0 in F1, 22.7 in F2, 22.85 in F3, 43.4 in F4, 48.4 in F5) and HAI score (median was 19.1 in minimal, 21.4 in mild, 32.55 in moderate and 48.7 in severe) compared to children lower degrees. While there was no statistical difference regarding to type of cells (Figure 2).

Adiponectin had a statistically significant positive correlation with (TB, DB, AST, ALT, ALP, GGT, PT, PTT, INR, APRI score, FIB-4, Child-Pugh, PELD and MELD) and statistically negative correlation with (hemoglobin, platelets, albumin) (Table 4). There was no statistical difference in adiponectin level as regarding to patients' sex, consanguinity, family history of CLDs and different etiologies of CLD (Table 5).

The performance of adiponectin in the detection of cases of CLD with mild to moderate fibrosis (F1-F2) from controls was evaluated using ROC analysis. The AUC was 0.998 (95% confidence interval: 0.993-1), with a p-value of less than 0.001. The sensitivity was 94% and the specificity was 98% at a cutoff point exceeding 12.5 μg/mL. The performance of adiponectin in detecting cases of extensive fibrosis (F5-F6) was evaluated using ROC analysis. The AUC was 0.969 (95% confidence interval: 0.918-1), with a p-value of less than 0.001. The sensitivity was 91% and the specificity was 89.9% at a cutoff point exceeding 29.4 μg/mL (table 6 & figure 3,4)

Table 1: Clinical criteria in the studied patients.

		CLD group N=50	%
Age of disease onset (years)	**Mean ±SD**	3.1±1.7	
	Range	0-11	
Disease duration (years)	**Mean ±SD**	7.4±1.9	
	Range	1-10	
Etiology of chronic liver disease	**Autoimmune hepatitis**	14	28.0%
	Chronic hepatitis B	2	4.0%
	Chronic hepatitis C	5	10.0%
	Congenital hepatic fibrosis	2	4.0%
	Glycogen storage disease	20	40.0%
	NASH due to Abeta lipoproteinemia	٢	.0%٤
	Wilson disease	5	10.0%
Main complaint	**Abdominal distension**	15	30.0%
	Abdominal pain	12	24.0%
	Jaundice	8	16.0%
	Anorexia, fatigue	6	12.0%
	Hypoglycemia and convulsions	9	18.0%

Table 2: Laboratory investigations of the studied groups

		CLD group N=50 %	Control group N=50 %	Test	P value
Hemoglobin (mg/dl)	**Mean ± SD**	10.1±1.2	11.8±0.9	t=6.7	<0.001*
	Range	7.9-12.5	10.5-13.2		
WBCs (x10^3 /L)	**Mean ± SD**	7.3±3.1	7.2±2.5	t=0.67	0.51
	Range	4-12	4.5-11.2		
Platelets (x10^3/L)	**Mean ± SD**	161±96	246±61	t=5.8	<0.001*
	Range	91-310	227-440		
AST (U/L)	**Median**	50	28.5	U=5.7	<0.001*
	IQR	42-123	20-31		
ALT (U/L)	**Median**	73.4	28	U=5.4	<0.001*
	IQR	50-124	19-31		
ALP (U/L)	**Median**	251	214	U=4.3	<0.001*
	IQR	233-430	198-251		
GGT (U/L)	**Median**	37	23	U=4.9	<0.001*
	IQR	33-53	21-28		
Total bilirubin (mg/dl)	**Mean ± SD**	1.4±0.7	0.7±0.2	U=6.3	<0.001*
	Range	0.5-5.1	0.2-1		
Direct bilirubin (mg/dl)	**Mean ± SD**	1.1±0.5	0.2±0.1	U=2.2	0.027*
	Range	0.2-2.9	0.1-0.3		
Serum albumin (g/dl)	**Mean ± SD**	3.7±0.4	4.1±0.3	t=1.8	0.061
	Range	3-4.8	3.5-5.4		
PT (sec.)	**Mean ± SD**	13.3±2.2	12.5±0.7	t=3.4	<0.001*
	Range	11-16	11-14		
PTT (sec.)	**Mean ± SD**	38.2±6.4	30.1±2.5	t=3.2	<0.001*
	Range	30-47	26-40		
INR	**Mean ± SD**	1.3±0.1	1.1±0.1	t=2.9	<0.001*
	Range	1-1.5	0.9-1.1		

t: Student t-test, U: Mann-Whitney U test, *: significant, WBCs: white blood cells, ALT: alanine aminotransferase, AST: aspartate aminotransferase, ALP: alkaline phosphatase, GGT: Gamma Glutamyl Transferase, PT: prothrombin time, PTT: Partial thromboplastin time, INR: international normalized ratio

Table 3: Liver biopsy results in the studied group according to Ishak score

		CLD group N=50	%
Degree of fibrosis	**No fibrosis (F0)**	4	8.0%
	Mild (F1)	21	42.0%
	Mild to Moderate (F2)	8	16.0%
	Moderate fibrosis (F3)	10	20.0%
	Moderate to severe fibrosis (F4)	5	10.0%
	Incomplete cirrhosis (F5)	2	4.0%
	Cirrhosis (F6)	0	0.0%
	Mean ±SD (/6)	1.7±0.9	
	Range	0-5	
Histological activity index	**Minimal**	21	42.0%
	Mild	17	34.0%
	Moderate	6	12.0%
	Severe	6	12.0%
	Mean ±SD (/18)	4.8±2.9	
	Range	1-16	
Type of cells	**Diffemploye ballooning degeneration, intralobular fatty infiltration**	5	10.0%
	Lymphocytes	16	32.0%
	Eosinophils	3	6.0%
	Mononuclear inflammatory cells	24	48.0%
	Steatosis	2	4.0%

Table 4: Correlation between adiponectin and other clinical data of the studied patients

	Adiponectin (µg/mL) r	P value
Age (years)	0.060	0.552
Weight percentile	0.175	0.121
Height percentile	0.168	0.189
BMI percentile	0.132	0.236
Hemoglobin (mg/dl)	-0.569	<0.001*
WBCs (x10^3 /L)	-0.019	0.850
Platelets (x10^3/L)	-0.552	<0.001*
Total bilirubin (mg/dl)	0.611	<0.001*
Direct bilirubin (mg/dl)	0.245	0.016*
AST (U/L)	0.497	<0.001*
ALT (U/L)	0.484	<0.001*
ALP (U/L)	0.246	0.014*
GGT (U/L)	0.570	<0.001*
PT (sec.)	0.309	0.002*
PTT (sec.)	0.253	0.011*
INR	0.446	<0.001*
Serum albumin (g/dl)	-0.214	0.033*
APRI Score	0.448	<0.001*
FIB-4	0.338	0.001*
Child-Pugh	0.422	<0.001*
PELD	0.392	<0.001*
MELD	0.345	0.006*

r: Correlation coefficient, *: significant, WBCs: white blood cells, ALT: alanine aminotransferase, AST: aspartate aminotransferase, ALP: alkaline phosphatase, GGT: Gamma Glutamyl Transferase, PT: prothrombin time, PTT: Partial thromboplastin time, INR: international normalized ratio,

Table 5: Adiponectin level as regarding to patients' clinical criteria.

		Adiponectin (µg/mL)		Test	P value
		Median	IQR		
Sex	**Male**	21.60	19.1-22.6	U=0.03	0.97
	Female	22.70	18.4-27.8		
Consanguinity	**Negative**	22.25	19.1-25.9	U=0.31	0.74
	Positive	21.00	19.2-25.7		
Family history of CLDs	**Negative**	21.16	19.2-24.2	U=1.3	0.07
	Positive	23.15	18.10-29.90		
Etiology of chronic liver disease	**Autoimmune hepatitis**	23.95	20.20-28.80	W=7.2	0.08
	chronic hepatitis b	24.40	25.70-43.10		
	chronic hepatitis c	18.10	14.20-22.50		
	congenital hepatic fibrosis	19.20	17.9-26.5		
	glycogen storage disease	21.40	20.20-28.20		
	NASH due to Betalipoproteinaemia	28.20	21.8-31.5		
	Wilson disease	19.20	19.10-32.90		

U: Mann-Whitney U test, W: Wilcoxon signed-rank test

Table 6: Performance of adiponectin to detect cases of CLD with mild to moderate fibrosis (F1-F3) and cases of severe fibrosis (F4- F6) from controls.

Adiponectin (µg/mL)	**AUC**	**95% CI**		**Cut-off value**	**Sensitivity**	**Specificity**	**P value**
Mild to moderate fibrosis (F1-F2)	0.998	0.993	1	≥12.5	94%	98%	<0.001*
Severe fibrosis (F4-F6)	0.969	0.918	1	≥29.4	91%	89.9%	<0.001*

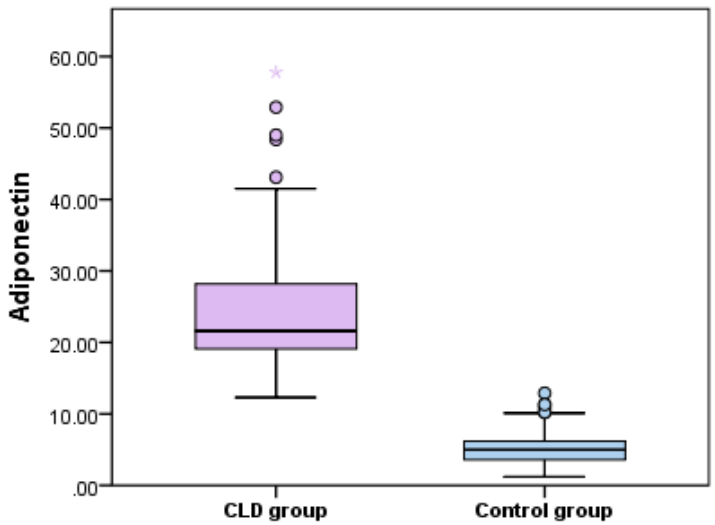

Figure 1: Adiponectin level in the studied group

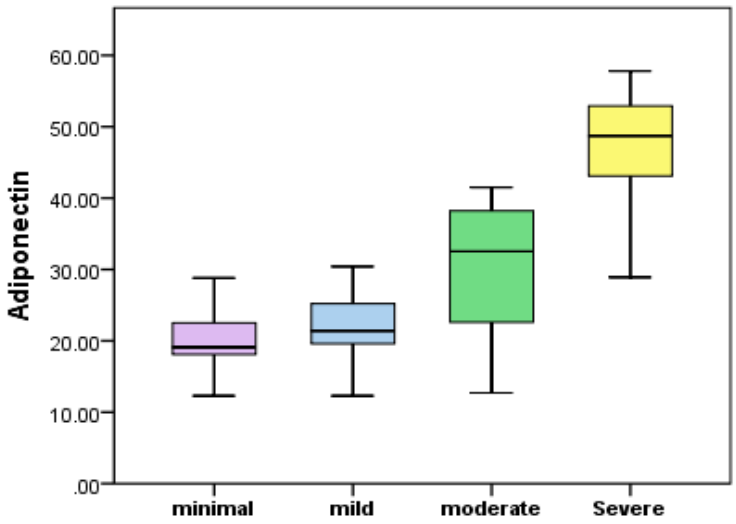

Figure 2: Adiponectin level as regarding to HAI score.

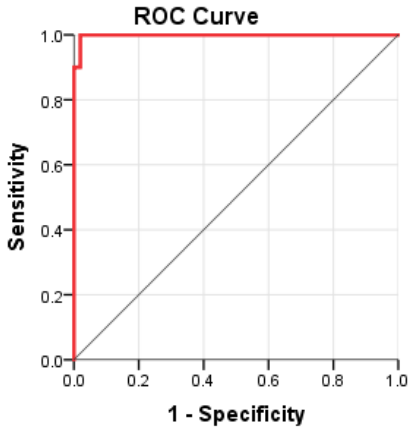

Figure 3: ROC curve of performance of adiponectin to detect cases of CLD with mild to moderate fibrosis (F1-F2) from controls.

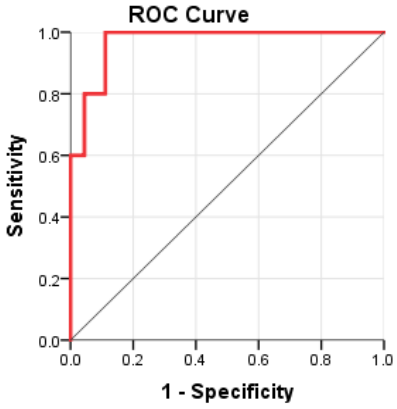

Figure 4: ROC curve of performance of adiponectin to detect cases of severe fibrosis (F5-F6) from controls.

Discussion

An anti-inflammatory function of adiponectin is exhibited in both acute and chronic inflammatory liver disorders. Presence of elevated plasma adiponectin titers may indicate a discrepancy between adipocyte synthesis and liver metabolism. One sign of the body's anti-inflammatory response to CLD is elevated adiponectin titers. Becaemploy the liver is so important for catabolism, increased plasma titers in cirrhosis are partly caemployd by reduced hepatic catabolism. Researchers have shown that hepatocytes express high tires of adiponectin mRNA following damage, suggesting that actual hepatic synthesis could have an additional effect. Adiponectin is produced by dormant hepatic stellate cells (HSCs), and it can put active HSCs to death and prohibit their growth. Another explanation for the elevated adiponectin titters in cirrhosis of the liver is alterations in hepatic extraction. It appears that the underlying caemploy has no effect on the elevated titers of circulating adiponectin in cirrhosis [8].

In the current study, CLD group had statistically significant higher adiponectin compared to control group. Our results was in agreement with Udomsinprasert and co-authors [9], The researchers discovered that BA patients' serum adiponectin concentrations were significantly greater than those of the healthy controls ($p<0.001$).

There is shortage of the investigations who assessed adiponectin in children with CLDs. Researchers have looked at adiponectin's function in liver fibrosis in adults. All of the investigations have exhibited that cirrhotic patients have higher titers of systemic adiponectin than controls [10–12]. Carvalho and co-authors [11], reported that HCV infected cases had higher adiponectin titers,

Our results runs in accordance with Balmer and co-authors [13], The results of their study suggested that the serum adiponectin titers of cirrhotic patients were significantly higher than those of patients with other liver disorders. The levels of blood adiponectin in individuals with CLD were exhibited to be associated with surrogate markers of liver fibrogenesis, including transient elastography, fasting serum bile acids, and hyaluronate. These markers serve as indirect indicators of the extent of liver fibrosis and its progression in CLD patients.

And recently, Ismaiel and co-authors [14], who conducted research on Adiponectin as a biomarker in liver cirrhosis, A systematic review and meta-analysis exhibited that compared to controls, liver cirrhosis is linked to higher titers of adiponectin in both serum and plasma.

This elevation is associated with advanced liver injury, systemic inflammation, and metabolic alterations in cirrhosis, which supports the potential of adiponectin as a biomarker for distinguishing cirrhosis from other CLD [15].

da Silva and co-authors [10], who noted that patients with cirrhosis exhibited a higher level of adiponectin (21.59 μg/mL vs. 12.52 μg/mL, $P < 0.001$) than controls.

Emerging evidence underscores the anti-inflammatory role of adiponectin in both acute and chronic inflammatory liver diseases. Elevated plasma adiponectin levels observed in CLD may reflect a disruption between its production by adipocytes and its hepatic metabolism. This elevation could represent an adaptive, anti-inflammatory mechanism within the body, aiming to counteract the ongoing inflammatory process. The liver plays a pivotal role in adiponectin catabolism, and in cirrhosis, reduced hepatic clearance contributes to the heightened plasma levels. In addition, hepatocytes, particularly following injury, have been shown to significantly express adiponectin mRNA, further suggesting that the liver itself contributes to the increased adiponectin in circulation. Furthermore, HSCs, in their quiescent state, produce adiponectin, which may help regulate HSC behavior by inducing apoptosis and inhibiting their proliferation in response to

injury. Another potential factor driving the elevated adiponectin levels in cirrhosis is altered hepatic extraction, with studies suggesting that these increased levels are not influenced by the underlying etiology of the liver disease. Thus, the elevated plasma adiponectin in cirrhosis may reflect complex shifts in hepatic metabolism, cellular responses, and inflammatory regulation [8].

While previous clinical investigations have exhibited a direct correlation between adiponectin levels and liver fibrogenesis in patients with various CLDs, the exact mechanism behind the elevation of circulating adiponectin in liver fibrosis remains unclear. One explanation for this phenomenon may lie in the reduced clearance of adiponectin. In CLD patients with liver fibrosis, impaired adiponectin clearance could result from diminished uptake by liver sinusoidal endothelial cells (LSECs), potentially leading to elevated adiponectin levels in the bloodstream. It is well-established that LSEC dysfunction plays a crucial role in liver fibrogenesis. In a healthy liver, LSECs maintain HSCs quiescence. However, during liver fibrosis, LSECs undergo phenotypic changes, which include the loss of key receptors and the disruption of their fenestration, resulting in the capillarization of liver sinusoids. This alteration impairs the normal uptake of various substances. Studies have shown that adiponectin levels and the expression of its receptor, adipoR2, are reduced in LSECs following liver injury. These alterations may provide insight into the observed hyperadiponectinemia in patients with liver fibrosis associated with CLDs. [12].

Lucero and co-authors [16], We measured the titers of systemic adiponectin in 36 people with metabolic syndrome and 24 patients with non-alcoholic fatty liver disease. Metabolic syndrome was associated with a higher adiponectin level in NAFLD patients. Those who suffered from non-alcoholic fatty liver disease had metabolic parameters, circulating adiponectin titers, and liver fibrosis severity that interacted within certain ranges.

In the current study, there was no statistical difference in adiponectin level as regarding to patients' sex, consanguinity, family history of CLDs or different etiologies of CLD. Adiponectin was statistically significant higher in children with higher degree of fibrosis and HAI score compared to children's lower degrees.

da Silva and co-authors [10], Adiponectin titers were discovered to be correlated with the severity of hepatic dysfunction in patients with CLD.

In the same way, Udomsinprasert and co-authors [9] In their examination of the correlation between circulating adiponectin titers and clinical parameters in patients with BA, specifically liver stiffness scores, the researchers observed that serum adiponectin concentrations were significantly higher in patients with significant liver fibrosis than in those with insignificant fibrosis. In addition, the severity of hepatic fibrogenesis was directly correlated with serum adiponectin titers. Forty healthy controls and 106 patients with BA were included in the investigation.

There needs to be more investigation into the role of adiponectin in liver fibrosis progression becaemploy the fact that viral hepatitis and cirrhosis do not differ in blood adiponectin titers suggests that the two diseases share similar inflammatory mechanisms and severity of disease [17].

Adiponectin exhibited a statistically significant positive correlation with the following: TB, DB, AST, ALT, ALP, GGT, PT, PTT, INR, APRI score, FIB4, Child-Pugh, PELD, and MELD. Conversely, adiponectin exhibited a statistically negative correlation with hemoglobin, platelets, and albumin.

Similarly, da Silva and co-authors [10], TB and adiponectin titers were positively correlated (P = 0.015), whereas albumin and body mass index were negatively

correlated (P = 0.024 and P = 0.002, respectively). Child-Pugh A subjects had considerably lower adiponectin titers (30.47 µg/mL vs. 17.04 µg/mL, P = 0.008) when contrasted with Child-Pugh B/C subjects. Likewise, patients with MELD scores greater than 10 had higher adiponectin titers (25.67 µg/mL vs. 19.07 µg/mL, P = 0.017). In contrast, adiponectin titers were unaffected by factors including dietary status and present alcohol employment.

Our results were also matched with Udomsinprasert and co-authors [(9)], who revealed that serum adiponectin exhibited a positive correlation with serum AST (r = 0.626, p <0.001), ALT (r = 0.344, p <0.001), ALP (r = 0.335, p = 0.001), and TB (r = 0.626, p <0.001). In addition, serum adiponectin titters were positively correlated with the extent of liver fibrosis in patients with BA.

This was also in agreement with Salman and co-authors [(8)]**,** who noted that the clinical stage of cirrhosis in comparison to controls influenced the increases in circulating adiponectin. Also, aminotransferase activities, which are indicators of liver cell injury, paradoxically correlated with an increase in adiponectin. Laboratory markers of cholestasis (bilirubin, alkaline phosphatase, and GGT) were also associated with it. This suggests that, because of reduced biliary excretion, adiponectin may be elevated in cholestasis. As a biomarker for liver cirrhosis, adiponectin may help in determining the severity of the disease by depicting the interplay between dysfunctional adipose tissue, inflammation, and metabolic abnormalities [(18)]**.**

Following confirmation of its effectiveness, adiponectin can serve as a convenient and non-invasive biomarker for the early diagnosis of liver cirrhosis, risk stratification, and the tracking of disease progression. This could result in improved patient outcomes and a reduction in the necessity for invasive procedures [(14)]**.**

Limitations of the study

This study was limited by the small sample size which did not allow a better analysis. Also, this was a cross-sectional study, so role of adiponectin as a prognostic factor could not be assessed.

Conclusion

In children with CLDs, these findings point to the possibility of adiponectin as a noninvasive biochemical marker for assessing the extent of liver fibrosis. To enhance the diagnostic accuracy of adiponectin, evaluate its function in treatment decisions, and ascertain its value in conjunction with other biomarkers for more accurate prognostic evaluations, further research is necessary.

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