Menoufia Medical Journal

PRINT ISSN: 1110-2098 - ONLINE ISSN: 2314-6788

journal hompage: www.menoufia-med-j.com

Volume 36 | Issue 1 Article 13

2023

Plasma pentraxin 3 as novel diagnostic marker in nonalcoholic fatty liver disease

El Sayed Ibrahium El Shayeb
Department of Internal Medicine, Gastroenterology and Hepatology, Faculty of Medicine Menoufia University, Egypt

Eman Masoud Abd El Gayed
Department of Medical Biochemistry & Molecular Biology, Faculty of Medicine, Menoufia University, Menoufia, Egypt

Janet George Hanna Sedhom
Department of Internal Medicine, Gastroenterology and Hepatology, Faculty of Medicine Menoufia University, Egypt, janet.george.salam6@gmail.com

Abd EL Naser Abdel Atty Gadallah
Department of Internal Medicine, Gastroenterology and Hepatology, Faculty of Medicine Menoufia University, Egypt

Recommended Citation

El Shayeb, El Sayed Ibrahium; El Gayed, Eman Masoud Abd; Sedhom, Janet George Hanna; and Gadallah, Abd EL Naser Abdel Atty (2023) "Plasma pentraxin 3 as novel diagnostic marker in nonalcoholic fatty liver disease," *Menoufia Medical Journal*: Vol. 36: Iss. 1, Article 13.
DOI: https://doi.org/10.59204/2314-6788.1012

ORIGINAL STUDY

Plasma Pentraxin 3 as a Novel Diagnostic Marker in Nonalcoholic Fatty Liver Disease

El Sayed I. El Shayeb [a], Eman M. Abd El Gayed [b], Janet G.H. Sedhom [a,*], El Naser A. Gadallah [a]

[a] Departments of Internal Medicine, Gastroenterology and Hepatology, Egypt
[b] Departments of Medical Biochemistry & Molecular Biology, Faculty of Medicine, Menoufia University, Menoufia, Egypt

Abstract

Objective: **To assess the role of plasma pentraxin 3 (PTX-3) in nonalcoholic fatty liver disease (NAFLD) among Egyptian patients.**

Background: **NAFLD is a serious health concern and amounts to significant burden on health care systems.**

Patients and methods: **A randomized controlled trial was conducted on 90 participants at the outpatient clinic and inpatient Internal Medicine Departments, Menoufia University Hospitals. All included participants were divided into 70 patients with NAFLD and 20 control healthy persons. Blood pressure, weight, height, BMI, waist circumference, fasting blood glucose, prothrombin time, activated partial prothrombin time, international normalized ratio, liver enzymes, lipid profile, and PTX-3 level were investigated.**

Results: **There were significantly higher PTX-3 levels in both steatohepatitis and steatosis groups than the control group ($P < 0.001$). Moreover, patients with steatosis had significantly higher PTX-3 levels than the control group ($P < 0.001$). Receiver operating characteristic curve analysis showed that PTX-3 is an excellent diagnostic marker in predicting steatosis cases from a healthy free cohort at a cut-off point more than 2.7745, with sensitivity 97%, specificity 75%, and area under the curve of 98%.**

Conclusion: **Patients with steatohepatitis and steatosis showed significant increased PTX-3 levels with a significant positive correlation with respect to PTX-3 levels, BMI, and cholesterol levels when compared with the control group.**

Keywords: Egyptian patients, Hepatitis C viral, Nonalcoholic fatty liver disease, Plasma pentraxin 3, Waist circumference

1. Introduction

Nonalcoholic fatty liver disease (NAFLD) is a growing public health problem worldwide, which represents a serious health concern and will amount to significant burden on health care systems. It is increasingly recognized as the liver disease component of metabolic syndrome [1]. It is a disease spectrum consisting of the benign nonalcoholic fatty liver (NAFL) and nonalcoholic steatohepatitis (NASH), which is a more progressive form of NAFLD characterized by steatosis, hepatocellular ballooning, lobular inflammation, and almost always fibrosis. The progression of NASH to cirrhosis may lead to hepatocellular carcinoma [2].

Over the past couple of decades, it has become increasingly clear that NAFLD and NASH are now the number one causes of liver disease in Western countries. The prevalence of NAFLD has doubled during last 20 years, whereas the prevalence of other chronic liver diseases has remained stable or even decreased. More data confirm that NAFLD and NASH play an equally important role in the Middle East, Far East, Africa, the Caribbean, and Latin America [3].

Pentraxin 3 (PTX-3) (an acute-phase protein) is a member of the long pentraxin protein family. Cabiati et al. [4] reported that PTX-3 is significantly associated with obesity, metabolic syndrome, and cardiovascular diseases.

Received 22 October 2022; accepted 21 December 2022.
Available online 15 May 2023

* Corresponding author at: El-Zaytoun, Cairo, 11725, Egypt.
E-mail address: janet.george.salam6@gmail.com (J.G.H. Sedhom).

https://doi.org/10.59204/2314-6788.1012

Pentraxins are proteins formed by five monomers that form a ring in radial symmetry. They are a class of pattern recognition receptors. Among pentraxins, the main ones are PTX-3, C-reactive protein (CRP), and serum amyloid P component. PTX-3 is a long-chain pentraxin considered an acute-phase marker, produced mainly by endothelial and vascular smooth muscle cells at the site of inflammation. This was also produced by macrophages, fibroblasts, neutrophils, epithelial cells, dendritic cells, and other cell types both near and far from the inflammation site [5].

PTX-3 has been recognized as an independent marker of inflammation associated with various disorders such as atherosclerosis, cancer, respiratory diseases, and central nervous system diseases in which increased levels are related to the risk of the disease or its progression. However, the role of PTX-3 in the hepatic disorders such as NAFLD needs more clarification [6].

PTX-3 was recently characterized as a novel vascular-specific inflammatory biomarker that correlated with several components constituting the metabolic syndrome, implicated in atherosclerosis, and used for cardiovascular risk assessment. Several clinical epidemiological studies have been published demonstrating the relationship between plasma PTX-3 levels and increased risk of cardiovascular disease [7]. The aim of this study was to assess the role of plasma PTX-3 in NAFLD among Egyptian patients.

2. Patients and methods

2.1. Methods

This is a randomized controlled trial that was conducted on 90 participants at outpatient clinic and inpatient Internal Medicine Departments, Menoufia University Hospitals. All participants were divided into three groups: group I included 35 patients with simple steatosis (non-NASH), group II included 35 patients with steatohepatitis (NASH), and group III included 20 age-matched and sex-matched healthy participants as the control group.

Ethical consideration: all procedures were carried out in accordance with the ethical standards of the institutional committee. The study received the approval of ethical committee of Menoufia University Hospitals. A written informed consent was taken from all included participants after explaining the aim of the study.

Inclusion criteria were patients aged more than 18 years, who had abnormal serum transaminases and had one or more of the following features of metabolic syndrome: (a) fasting blood glucose more than 110 mg/dl or a previous diagnosis of diabetes mellitus, (b) BMI of 27 or higher or waist circumference (WC) more than 102 cm in males and 88 cm in females, (c) blood pressure more than 130/85 or current antihypertensive treatment, (d) triglyceride (TG) levels more than 150 mg/dl or current use of fibrates, and (e) high-density lipoprotein (HDL)-cholesterol less than 40 mg/dl (males) and 50 mg/dl (females). A total of 70 patients were included. We excluded patients who did not have a history of any hepatotoxic drugs, hormone replacement therapy nor herbal products, no alcohol consumption more than 20 g/day, and no history of previous liver diseases (no viral or autoimmune hepatitis, hemochromatosis, Wilson's disease, alpha-1 antitrypsin deficiency, biliary disease, nor malignancies).

All participants included in this study were subjected to the following: full history taking as age, sex, and history of disease; thorough clinical examination such as blood pressure, weight, height, BMI, and WC; and laboratory investigations, including complete blood count, liver enzymes tests [alanine aminotransferase (ALT) and aspartate aminotransferase (AST)], lipid profile [TGs, HDL, low-density lipoprotein (LDL), and cholesterol], fasting blood glucose, prothrombin time (PT), activated partial prothrombin time, international normalized ratio (INR), and biochemical measurement of plasma PTX-3 level using enzyme-linked immunosorbent assay kit (2021; Shanghai Sunred Biological Technology Co. Ltd, Shanghai, China).

Test principle: to assay the level of human PTX-3 in the samples, PTX-3 was added to monoclonal antibody enzyme well, which was precoated with human PTX-3 monoclonal antibody, followed by incubation. Then, PTX-3 antibodies labeled with biotin were added and combined with streptavidin–HRP to form an immune complex. Then, incubation was carried out followed by wash to remove the uncombined enzyme. Then, chromogen solutions A and B were added, and the color of the liquid changed in the blue. With the effect of acid, the color finally became yellow.

The kit uses a double-antibody sandwich enzyme-linked immunosorbent assay to assay the level of human PTX-3 in samples.

Conventional ultrasonography used for screening of suspected NAFLD, owing to its lack of invasiveness, wide availability, and relatively low cost. NAFLD sonographic features include increased echogenicity ‘bright liver,’ hepatomegaly, and intrahepatic vascular blurring. Steatosis is reported to be detectable by ultrasound when more than 20% of hepatocytes contain histologically visible fat

droplets, with a reported sensitivity of 79.7% and specificity of 86.2% [8]. Liver fibrosis scores included aspartate aminotransferase to platelet ratio index (APRI) score calculated by using the Wai's formula: (AST/upper limit of normal)/platelet count ($\times 10^9$/l) × 100 [9]. Fibrosis-4 score calculated by using the Sterling's formula [age (years) × AST (IU/l)/platelet count ($\times 10^9$/l) × (sqr (ALT)] (IU/l). The scoring system creates a score, where less than 1.45 has a negative predictive value of over 90% for advanced liver fibrosis, and a score of more than 3.25 has a positive predictive value of 65% for advanced fibrosis, with a specificity of 97% [10]. The NAFLD fibrosis score calculated by using the following formula: −1.675 + 0.037 × age (years)+0.094 × BMI (kg/m^2) +1.13 × IFG/diabetes (yes = 1 and no = 0)+ 0.99 × AST/ALT ratio−0.013 × platelet count ($\times 10^9$/l)−0.66 × albumin (g/dl) [11]. Göteborg University Cirrhosis Index (GUCI) was calculated using the following formula: ([AST/upper limits of normal] × INR × 100)/platelet count ($\times 10^9$/l) [12]. King's score was calculated using the following formula: age × AST × INR/PLT ($\times 10^9$/l) [13].

The aim of the research was to use PTX-3 as a diagnostic biomarker for NAFLD and correlate it with fibrosis scores, so fibroscan was not done for the patients.

2.2. Statistical analysis

Data collected throughout history, basic clinical examination, and outcome measures were coded, entered, and analyzed using Microsoft Excel software. Data were then imported into the Statistical Package for the Social Sciences (SPSS version 25.0) (2018; IBM Corp., Armonk, New York, USA). Descriptive statistics included percentage, mean, and SD and analytic statistics included χ^2 test, one-way analysis of variance (F test), Kolmogorov–Smirnov/Shapiro–Wilk tests, Mann–Whitney U, Student t test, and Kruskal–Wallis test. P value less than 0.05 was considered statistically significant.

3. Results

In the current study, the studied groups were matched regarding age, sex, and smoking habits ($P > 0.05$). A significant difference was found between the studied groups regarding BMI and WC ($P < 0.001$). Patients with steatohepatitis had significantly higher mean values of BMI than steatosis and control groups ($P < 0.001$). In addition, the steatosis group had significantly higher mean values of BMI than controls ($P < 0.001$). Patients with steatohepatitis had significantly higher mean values of WC than the control group ($P < 0.001$), and the steatosis group had significantly higher mean values of WC than the control group ($P < 0.001$). There were significant differences between the studied groups regarding all of the applied fibrosis scores ($P < 0.001$). The steatohepatitis group had significantly higher mean values of all scores (APRI score, FIB-4 score, GUCI, and King's score) than both steatosis and control groups ($P < 0.001$) (Table 1).

Moreover, patients with steatohepatitis had significantly higher ALT, AST, ALP, creatinine, and LDL than the steatosis group ($P < 0.05$). However, a significantly lower value of albumin and HDL was recorded among patients with steatohepatitis than patients with steatosis. Moreover, patients with steatohepatitis had significantly higher ALT, AST, GGT, cholesterol, TG, and LDL but had lower ALP, albumin, and HDL than the control group ($P < 0.05$). In this concern, a significant difference found between the studied groups regarding abdominal-pelvic ultrasonography findings; both steatohepatitis and steatosis groups showed bright liver and had higher mean liver size than the control group. Moreover, patients with steatohepatitis had higher mean liver size than the steatosis group ($P < 0.05$). Additionally, there were significantly higher median values of PTX-3 in both steatohepatitis and steatosis groups than the control group ($P < 0.001$). Moreover, patients with steatosis had significantly higher median values of PTX-3 levels than the control group ($P < 0.001$) (Table 2).

Additionally, there was a significant positive correlation between PTX-3 levels and BMI among patients with steatohepatitis ($r = 0.35$, $P = 0.038$). In this respect, there was a significant positive correlation between PTX-3 levels and cholesterol levels ($r = 0.47$, $P = 0.038$) among the control group (Table 3).

Receiver operating characteristic (ROC) curve analysis showed that PTX-3 is an excellent diagnostic marker in predicting NAFL cases from healthy controls at a cutoff point more than 2.815, with sensitivity of 99%, specificity of 85%, and area under the curve of 99% (Table 4 and Fig. 1).

4. Discussion

NAFLD was one of the most common forms of chronic liver diseases among obese patients and as one of the features of the metabolic syndrome. It was characterized by accumulation of large TG droplets within the liver cells [6]. Serum PTX-3 level increased rapidly in inflammatory conditions, reaching its peak values after 6–8 h of any inflammatory condition; its elevation on the early phase is

Table 1. Demographic characteristic and fibrosis scores of the studied groups.

Demographic characteristic	Steatohepatitis ($N = 35$)	Steatosis ($N = 35$)	Controls ($N = 20$)	ANOVA F test	P value
Age (years)					
Mean ± SD	42.43 ± 13.16	44.91 ± 13.43	8.00 ± 10.53	1.87	0.160
Sex [n (%)]					
Male	15 (42.9)	18 (51.4)	10 (50.0)	$\chi^2 = 0.57$	0.753
Female	20 (57.1)	17 (48.6)	10 (50.0)		
BMI (kg/cm^2)	35.26 ± 3.81	28.37 ± 1.42	23.06 ± 1.05	151.23	<0.001[a]
Mean ± SD	$P1<0.001$, $P2<0.001$, $P3<0.001$				
WC (cm)	106.94 ± 9.34	106.26 ± 10.54	82.00 ± 8.80	49.87	<0.001[a]
Mean ± SD	$P1 = 0.076$, $P2<0.001$, $P3<0.001$				
Smoking habits [n (%)]					
Smoker	15 (42.9)	16 (45.7)	9 (45.0)	$\chi^2 = 0.06$	0.970
Nonsmoker	20 (57.1)	19 (54.3)	11 (55.0)		
APRI score	1.18 ± 0.22	0.29 ± 0.06	0.26 ± 0.01	422.61	<0.001[a]
	$P1<0.001$, $P2<0.001$, $P3 = 0.385$				
FIB-4 score	1.89 ± 0.60	0.79 ± 0.26	0.64 ± 0.19	82.21	<0.001[a]
	$P1<0.001$, $P2<0.001$, $P3 = 0.200$				
GUCI	1.29 ± 0.37	0.30 ± 0.07	0.28 ± 0.06	194.04	<0.001[a]
	$P1<0.001$, $P2<0.001$, $P3 = 0.792$				
King's score	20.27 ± 6.25	3.18 ± 0.25	2.62 ± 0.17	145.30	<0.001[a]
	$P1<0.001$, $P2<0.001$, $P3 = 0.227$				

ANOVA, analysis of variance; APRI score, AST to platelet ratio index; FIB-4, fibrosis-4; GUCI, Goteborg University Cirrhosis Index; WC, waist circumference.
χ^2, χ^2 test.
$P1$: steatohepatitis group compared with the steatosis group.
$P2$: steatohepatitis group compared with the control group.
$P3$: steatosis group compared with the control group.
[a] Significant.

due to rapid release of stored PTX-3 by the activated neutrophils [14]. The short pentraxins, CRP, and serum amyloid protein were produced by the liver as a systemic response to local inflammation, whereas expression of the long PTX-3 is induced by the damaged tissues [14].

Assessment of the potential of PTX-3 as a noninvasive tool for the detection and grading of NAFLD among Egyptian patients was highlighted as a main point of interest [15]. Consequently, this study was conducted and aimed to investigate the clinical usefulness of plasma PTX-3 levels to predict NAFLD. This case–control study was conducted at a tertiary care hospital at El-Menoufia University Hospitals and was performed on 70 adult patients with NAFLD and 20 normal healthy persons. During this study, 92 patients with NAFLD were assessed for eligibility, and 70 adult patients with NAFLD were included in the study (35 in each group). Of all eligible patients, 14 patients were excluded from the study based on the inclusion criteria and eight patients refused to participate in the study.

The current study revealed that patients with steatohepatitis had significantly higher mean values of BMI and WC than steatosis and control groups, whereas the steatosis group had significantly higher mean values of BMI and WC than the control group. Later, similar findings were reported by other investigators. Hussein et al. [6] revealed that there was a statistically significant difference found among the three studied groups regarding weight, BMI, and WC, which were significantly high in the NASH group ($P < 0.0001$ for each parameter).

Regarding fibrosis scores, the current study results revealed that patients with steatohepatitis had significantly higher APRI, FIB-4, GUCI, and King's scores than both steatosis and control groups. Albitar et al. [15] revealed that none of FIB-4, ALT ratio, and APRI were significantly correlated to pentraxin level. In addition, ultrasound measurements of the right lobe of the liver were correlated with the degree of steatosis.

Moreover, the current study results revealed that there were significantly higher median values of PTX-3 in both steatohepatitis and steatosis groups than the control group. Moreover, patients with steatosis had significantly higher PTX-3 levels than the control group. These findings agree with results of previous studies done by Makhlouf et al. [14], who revealed that plasma levels of PTX-3 showed significantly higher values in both group I (patients with NAFLD) and group II (patients with NAFLD with HCV), when compared with group III (control), with no significant difference between patients with NAFLD with and without chronic HCV (groups I

Table 2. Comparison between the studied groups regarding biochemical data.

Biochemical data	Steatohepatitis ($N = 35$)	Steatosis ($N = 35$)	Controls ($N = 20$)	ANOVA test	P value
	Mean ± SD	Mean ± SD	Mean ± SD		
ALT (IU/l)	105.54 ± 15.40	42.66 ± 7.12	36.35 ± 8.44	356.89	<0.001[a]
	$P1<0.001$, $P2<0.001$, $P3 = 0.050$				
AST (IU/l)	116.60 ± 13.84	31.57 ± 3.89	28.50 ± 5.11	918.87	<0.001[a]
	$P1<0.001$, $P2<0.001$, $P3 = 0.242$				
BIL.T (mg/dl)	1.05 ± 0.09	1.03 ± 0.11	1.01 ± 0.10	1.04	0.357
BIL.D (mg/dl)	0.17 ± 0.09	0.14 ± 0.08	0.14 ± 0.08	0.847	0.432
ALk. P (IU/l)	109.34 ± 19.01	94.29 ± 22.06	132.40 ± 11.29	25.78	<0.001[a]
	$P1 = 0.001$, $P2<0.001$, $P3<0.001$				
GGT (IU/l)	34.49 ± 5.45	34.20 ± 6.30	30.60 ± 7.19	2.85	0.063
	$P1 = 0.484$, $P2 = 0.028$, $P3 = 0.041$				
Albumin (g/dl)	3.28 ± 0.32	3.40 ± 0.36	4.03 ± 0.42	30.27	<0.001[a]
	$P1 = 0.136$, $P2<0.001$, $P3<0.001$				
Creatinine (mg/dl)	0.97 ± 0.16	0.85 ± 0.21	0.88 ± 0.18	3.91	0.024[a]
	$P1 = 0.009$, $P2 = 0.069$, $P3 = 0.656$				
Urea (mg/dl)	33.94 ± 5.16	32.80 ± 6.18	31.65 ± 5.81	1.06	0.353
Cholesterol (mg/dl)	296.71 ± 34.26	294.63 ± 34.83	127.30 ± 19.61	216.89	<0.001[a]
	$P1 = 0.785$, $P2<0.001$, $P3<0.001$				
TG (mg/dl)	274.23 ± 50.39	268.06 ± 36.08	104.30 ± 18.12	137.87	<0.001[a]
	$P1 = 0.715$, $P2<0.001$, $P3<0.001$				
HDL (mg/dl)	31.43 ± 4.74	33.91 ± 5.68	36.60 ± 6.60	5.63	0.005[a]
	$P1 = 0.065$, $P2 = 0.001$, $P3 = 0.880$				
LDL (mg/dl)	152.03 ± 10.55	145.54 ± 13.74	83.05 ± 9.03	251.52	<0.001[a]
	$P1 = 0.022$, $P2<0.001$, $P3<0.001$				
INR	1.08 ± 0.16	1.04 ± 0.09	1.07 ± 0.08	0.961	0.387
Pentraxin 3 (ng/ml) Median (IQR)	4.72 (3.87–12.07)	3.15 (3.03–3.37)	2.64 (2.49–2.78)	KW = 74.89	<0.001[a]
	$P1<0.001$[a], $P2<0.001$[a], $P3<0.001$[a]				
Abdomeno-pelvic ultrasonography					
Bright liver [n (%)]	35 (100)	35 (100)	0	$\chi^2 = 0.00$	1.00
Liver size (cm)					
Mean ± SD	18.50 ± 0.87	16.75 ± 0.62	13.14 ± 0.82	306.93	<0.001
Post hoc	$P1<0.001$, $P2<0.001$, $P3<0.001$				

ANOVA, analysis of variance; ALK.P, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BIL.D, direct bilirubin; BIL.T, total bilirubin; GGT, gamma-glutamyl transferase; HDL, high-density lipid; KW, Kruskal–Wallis test; LDL, low density lipid; TG, triglyceride.

$P1$: steatohepatitis group compared with steatosis group.

$P2$: steatohepatitis group compared with control group.

$P3$: steatosis group compared with control group.

[a] Significant.

and II). This is also consistent with the study of Yoneda et al. [16], who revealed that PTX-3 levels were significantly higher in patients with NAFLD than healthy controls. Ozturk et al. [17] demonstrated that PTX-3 levels in patients with NAFLD with fibrosis were higher than that in patients with NAFLD without fibrosis and healthy participants. On the contrary, Maleki et al. [18] found no significant difference between NAFLD and healthy controls regarding plasma PTX-3.

Consequently, our study revealed that there was a significant positive correlation between PTX-3 levels and BMI in the steatohepatitis group. Moreover, a significant positive correlation was found between PTX-3 levels and cholesterol levels in the control group, whereas a significant positive correlation was found between PTX-3 levels and FIB-4 score in patients with steatohepatitis. In agreement with our results, Makhlouf et al. [14] revealed that there was a significant positive correlation between PTX-3 and each of BMI, WC, fasting blood glucose, serum TG, serum LDL, PCR for HCV, serum ALT, serum AST, total and direct bilirubin, and total cholesterol. However, a significant negative correlation was found between PTX-3 and each of HDL, serum albumin, and platelet count. In concordance with our results, Hussein et al. [6] revealed that PTX-3 level was positively correlated with weight, BMI, WC, ALT, AST, total bilirubin, GGT, CRP, ESR, cholesterol, LDL, and TG, whereas no statistically significant correlation was found between PTX-3 and other studied parameters. Similarly, Kardas et al. [19] found significantly higher concentrations of plasma PTX-3 in obese children and adolescents with metabolic syndrome and higher TG levels, and

Table 3. Correlations between pentraxin 3 levels and clinical and laboratory data of the studied groups.

Variables	Pentraxin 3 levels (ng/ml)					
	Steatohepatitis ($N = 35$)		Steatosis ($N = 35$)		Controls ($N = 20$)	
	rho	*P* value	rho	*P* value	rho	*P* value
Age (years)	0.24	0.168	0.08	0.636	−0.12	0.609
BMI (kg/cm^2)	0.35	0.038[a]	−0.31	0.0.07	−0.07	0.762
WC (cm)	0.15	0.070	−0.08	0.632	0.12	0.604
ALT (IU/l)	0.02	0.893	−0.12	0.511	0.24	0.313
AST (IU/l)	0.21	0.236	−0.13	0.474	0.34	0.142
BIL.T (mg/dl)	−0.27	0.115	0.08	0.637	0.25	0.288
BIL.D (mg/dl)	0.09	0.623	−0.05	0.789	0.39	0.090
ALk. P (IU/l)	−0.21	0.225	−0.10	0.579	−0.04	0.853
GGT (IU/l)	0.07	0.702	−0.08	0.656	−0.29	0.221
Albumin (g/dl)	0.20	0.254	−0.11	0.560	−0.32	0.174
Creatinine (mg/dl)	−0.25	0.154	−0.21	0.239	0.28	0.226
Urea (mg/dl)	−0.11	0.546	−0.03	0.888	0.41	0.076
Cholesterol (mg/dl)	−0.12	0.496	−0.10	0.577	0.47	0.038[a]
TG (mg/dl)	0.24	0.166	−0.03	0.884	−0.14	0.569
HDL (mg/dl)	−0.09	0.623	0.05	0.774	0.02	0.925
LDL (mg/dl)	0.20	0.252	0.02	0.922	0.11	0.638
INR	0.04	0.825	−0.13	0.471	0.02	0.950
HB (g/dl)	0.18	0.299	0.13	0.463	−0.01	0.997
Platelets ($\times 10^3$/l)	0.01	0.976	0.08	0.659	0.29	0.222
TLC ($\times 10^9$/l)	−0.07	0.671	0.17	0.327	−0.22	0.352
Liver size (cm)	−0.02	0.944	0.08	0.652	−0.17	0.480

ALK.P, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BIL.D, direct bilirubin; BIL.T, total bilirubin; GGT, gamma-glutamyl transferase; HB, hemoglobin; HDL, high-density lipid; INR, international normalized ratio; LDL, low-density lipoprotein; TG, triglyceride; TLC, total leukocyte count; WC, waist circumference.
Rho: Spearman correlation.
[a] Significant.

PTX-3 levels correlated negatively with HDL cholesterol in their study.

PTX-3 is directly produced by damaged tissues, and a rapid increase indicates inflammation [20]. Elevated PTX-3 concentrations are related to liver-associated pathological conditions such as liver infections, NAFLD, NASH, and hepatic tumors [21]. The persistent elevation in PTX-3 levels is associated with disease severity and increased morbidity in several clinical conditions. Persistently elevated PTX-3 may represent a novel and promising biomarker of liver disease [14].

According to the ROC analysis in our study, PTX-3 is an excellent diagnostic marker in predicting NAFL cases from healthy controls at a cutoff point more than 2.815, with sensitivity of 99%, specificity of 85%, and area under the curve of 99%. Similarly, Hussein et al. [6] constructed a ROC curve to assess the accuracy of PTX-3 level to detect NASH and non-NASH group and revealed that the best cutoff

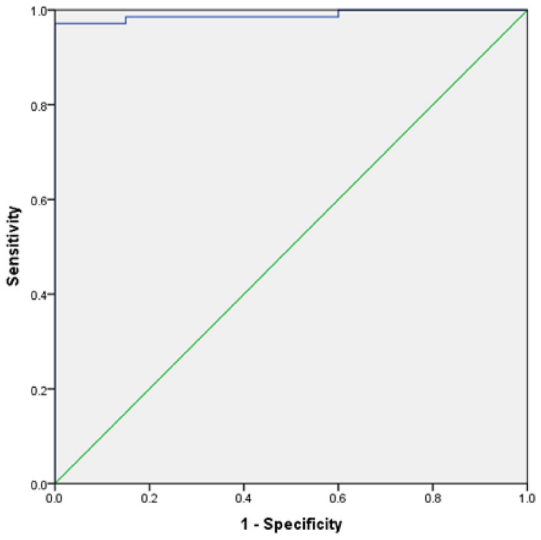

Fig. 1. Receiver operating characteristic (ROC) curve for pentraxin 3 levels in predicting NAFL (steatohepatitis + steatosis cases) versus controls. NAFL, nonalcoholic fatty liver.

Table 4. Sensitivity, specificity, cutoff points, and area under the curve of pentraxin 3 levels for prediction of nonalcoholic fatty liver cases from healthy controls.

Variables	Cut-off point	Sensitivity	Specificity	AUC	*P* value	95% CI (lower limit–upper limit)
Pentraxin 3 levels (ng/ml)	2.810	99%	85%	0.989	<0.001[a]	0.971–1.00

AUC, area under the curve; CI, confidence interval.
[a] Significant.

point between control group and non-NASH group regarding PTX-3 was more than 1.3, with sensitivity of 55%, specificity of 100%, and area under the curve of 74.7%, and the best cutoff point found between non-NASH and NASH groups regarding PTX-3 was more than 3.2, with sensitivity of 95%, specificity of 100%, and area under the curve of 99.4%.

The limitations of the study included blood samples could not be collected from obese persons in the same family because of genetic factors. Another limitation is the absence of liver biopsy and correlated histopathological results for confirmation of diagnosis of NAFLD.

4.1. Conclusion

The measurement of plasma PTX-3 is noninvasive and shows potential in identifying patients with NASH from patients with steatosis and healthy cohort, and it may serve as a clinical indicator of the degree of liver fibrosis in patients with NAFLD.

Conflict of interest

There are no conflicts of interest.

References

[1] Younossi ZM, Jarrar M, Nugent C, Randhawa M, Afendy M, Stepanova M, et al. A novel diagnostic biomarker panel for obesity-related non-alcoholic steatohepatitis (NASH). Obes Surg 2008;18:1430−7.
[2] Abdel-Rahman RF. Non-alcoholic fatty liver disease: epidemiology, pathophysiology, and an update on the therapeutic approaches. Asian Pac J Trop Biomed 2022;12:99.
[3] Wong WK, Chan WK. Non-alcoholic fatty liver disease: a global perspective. Clin Therapeut 2021;43:473−99.
[4] Cabiati M, Gaggini M, De Simone P, Del Ry S. Do pentraxin 3 and neural pentraxin 2 have different facet function in hepatocellular carcinoma? Clin Exp Med 2021;21:555−62.
[5] Kurts C, Ginhoux F, Panzer U. Kidney dendritic cells: fundamental biology and functional roles in health and disease. Nat Rev Nephrol 2020;16:391−407.
[6] Hussein A, Barrak M, El-monem A, El-Sayed Lashin H, Zied AE. Study of pentraxin-3 levels in non-alcoholic fatty liver disease (NAFLD) among Egyptian patients. Al-Azhar Med J 2022;51:495−506.
[7] Ristagno G, Fumagalli F, Bottazzi B, Mantovani A, Olivari D, Novelli D, et al. Pentraxin 3 in cardiovascular disease. Front Immunol 2019;10:823.
[8] Lee SS, Park SH. Radiologic evaluation of nonalcoholic fatty liver disease. World J Gastroenterol 2014;20:7392.
[9] Loaeza-del-Castillo A, Paz-Pineda F, Oviedo-Cárdenas E, Sánchez-Avila F, Vargas-Voracková F. AST to platelet ratio index (APRI) for the noninvasive evaluation of liver fibrosis. Ann Hepatol 2008;7:350−7.
[10] McPherson S, Hardy T, Dufour JF, Petta S, Romero-Gomez M, Allison M, et al. Age as a confounding factor for the accurate non-invasive diagnosis of advanced NAFLD fibrosis. Am J Gastroenterol 2017;112:740.
[11] Schmitz SM, Kroh A, Ulmer TF, Andruszkow J, Luedde T, Brozat JF, et al. Evaluation of NAFLD and fibrosis in obese patients a comparison of histological and clinical scoring systems. BMC Gastroenterol 2020;20:1−9.
[12] Shah RV, Allison MA, Lima JA, Bluemke DA, Abbasi SA, Ouyang P, et al. Liver fat, statin use, and incident diabetes: the Multi-Ethnic Study of Atherosclerosis. Atherosclerosis 2015;242:211−7.
[13] Cross ES, Hamilton AF, Kraemer DJ, Kelley WM, Grafton ST. Dissociable substrates for body motion and physical experience in the human action observation network. Eur J Neurosci 2009;30:1383−92.
[14] Makhlouf M, Saleh S, Rushdy M, Abdelhakam S, Abd-Elghani E. Pentraxin-3 in non-alcoholic fatty liver disease and its affection by concomitant chronic hepatitis C infection. Egypt Liver J 2019;9:1−8.
[15] Albitar AR, Emad N, Yamany A. Pentraxin 3 and non-alcoholic fatty liver disease in Egyptian patients: merits and flaws. Indian J Public Health Res Dev 2019;10:67.
[16] Yoneda M, Uchiyama T, Kato S, Endo H, Fujita K, Yoneda K, et al. Plasma pentraxin3 is a novel marker for nonalcoholic steatohepatitis (NASH). BMC Gastroenterol 2008;8:1−9.
[17] Ozturk K, Kurt O, Dogan T, Ozen A, Demirci H, Yesildal F, et al. Pentraxin 3 is a predictor for fibrosis and arterial stiffness in patients with non-alcoholic fatty liver disease. Gastroenterol Res Pract 2016;2016:1417962.
[18] Maleki I, Rastgar A, Hosseini V, Taghvaei T, Rafiei A, Barzin M, et al. High sensitive CRP and pentraxin 3 as non-invasive biomarkers of non-alcoholic fatty liver disease. Eur Rev Med Pharmacol Sci 2014;18:1583−90.
[19] Kardas F, Akõn L, Kurtoglu S, Kendirci M, Kardas Z. Plasma Pentraxin 3 as a biomarker of metabolic syndrome. Indian J Pediatr 2015;82:35−8.
[20] Kowdley KV, Belt P, Wilson LA, Yeh MM, Neuschwander-Tetri BA, Chalasani N, et al. Serum ferritin is an independent predictor of histologic severity and advanced fibrosis in patients with non-alcoholic fatty liver disease. Hepatology 2012; 55:77−85.
[21] Choi B, Chung EJ. Pentraxine 3 (PTX3) as a biomarker of liver disease. In: Preedy VR, editor. Biomarkers in liver disease: methods, discoveries, and applications. vol. 2. Biomedical and Life Sciences, Springer Nature, New York; 2016. p. 1−20.