The Accuracy of ABDA Score for the non-Invasive Identification of Fibrotic NASH in Egyptian Patients

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Background and study aim: The global incidence of non-alcoholic fatty liver disease (NAFLD) continues to rise annually, affecting 20-30% of the global population, which seriously impacts health particularly among individuals with metabolic syndrome. Non-alcoholic steatohepatitis (NASH) is a chronic liver inflammation that affects one-fifth of NAFLD patients. Fibrotic NASH is recognized as NASH with NAFLD activity score ≥4 with stage of fibrosis ≥2. Identifying those patients is crucial in view of the fact that they are at risk for complications, and may benefit from pharmacological treatment. Currently non-invasive tests have not been widely utilized for screening of fibrotic NASH. This study aimed to evaluate the accuracy of ABDA score in assessing fibrotic NASH in Egyptian patients.

Patients and Methods: 140 NAFLD subjects were divided into two groups according to FAST score (subjects with fibrotic NASH (FAST ≥ 0.67)). Biochemical tests and anthropometry were assessed. We used alanine aminotransferase, body mass index , age and presence of diabetes to calculate the ABDA score

Results: 140 subjects were included with a mean age of 48.4 years, 46.4% were males, 55% had metabolic syndrome, and 11.4% had fibrotic NASH. The ABDA score showed excellent diagnostic performance (AUC, 0.933) with adequate internal validity. An ABDA score >-2.678 identified fibrotic NASH with a sensitivity and specificity of 93.75% and 84.68%, respectively.

Conclusion: The ABDA score utilizes four available parameters and may be used to identify fibrotic NASH with high accuracy.

INTRODUCTION

NAFLD terminology was replaced by the newer one, metabolic-associated fatty liver disease (MAFLD) which is characterized by liver damage caused by metabolic stress. Dispersed lipid infiltration into hepatocytes is a hallmark of this disease. The prevalence of MAFLD is considerably higher in Egypt (47.5% vs. 25% globally), with 56.7% showing signs of fibrosis [1].

Neither the AASLD nor the EASL recommend community screening for NAFLD ،even though it is common and the main reason for liver transplantation in the US and Europe [2].

NASH affects 20% of NAFLD patients and is a chronic liver disease that can progress to cirrhosis, malignancy, or severe fibrosis. Fibrosis stage is the key determinant in categorizing NASH severity, fibrotic NASH (≥F2 fibrosis), or NASH-cirrhosis (F4 fibrosis). [3]. Since most people with NAFLD don't have any symptoms at all, hence the need for a more reliable method to early detect that group to prevent further progression of illness and complications [4].

Liver biopsy is still the most accurate way to diagnose fibrotic NASH; however, this procedure is not widely used in clinical practice due to its invasiveness and the risks it poses. Noninvasive scoring systems are another option [5].

Today, the most validated scores for detection of fibrosis in NAFLD, is the NAFLD fibrosis score (NFS), the FIB-4 score, and the BARD score. [6, 7]. Recently, three noninvasive scores—the FibroScan-aspartate aminotransferase (FAST) score [8], NIS4 (miR-34a-5p, alpha-2 macroglobulin, YKL-40, and glycated haemoglobin) [9], and MACK-3(hoMa, Ast, CK18) [10] have been developed to evaluate fibrotic NASH. These scores, however, are based on blood tests that are only available in highly specialized liver clinics or that need to be evaluated instrumentally using vibration-controlled transient elastography.

With a sensitivity of 90%, the FAST composite score can diagnose biopsy-proven fibrotic NASH (FAST ≥ 0.67), by integrating the values of the controlled attenuation parameter (CAP), liver stiffness measurement (LSM), and AST [8].

A prognostic model for fibrotic NASH called the ABDA score was recently established. It takes into account age, body mass index (BMI), diabetes, and alanine aminotransferase (ALT). The formula for this score is: 24.74 + 3.65*In (ALT) + 0.14*BMI + 1.41*Diabetes [presents (1)/absent (0)] + 0.05*Age [11].

The purpose of this study was to study the accuracy of the ABDA score in identifying fibrotic NASH (FAST score ≥0.67) in asymptomatic Egyptian individuals.

PATIENTS AND METHODS

This cross-sectional research was carried out

2.1 Study Design and Patients Selection

From November 2023 through April 2024, 140 adults with NAFLD were included in this cross-sectional study. The participants were selected from the Tanta Tropical Medicine Outpatient Clinic at Tanta Faculty of Medicine in Egypt. The American Association of Clinical Endocrinology (AACE) 2022 guidelines were followed for the NAFLD diagnosis. These guidelines include :

1. Hepatic steatosis can be detected non-invasively using the CAP measured by FibroScan.
2. Exclusion of other possible etiologies of chronic liver disease, including autoimmune liver disorders, hepatitis B or C, secondary fatty liver, and cancer within the last two years
3. Moderate alcohol intake (no more than 30 grams for men and 20 grams for women). [12[
4. Approval from the Tanta University Faculty of Medicine Ethical Committee (Approval Number: 36264PR491/1/24) each participant's signed informed consent was acquired.

After reviewing and accepting the final manuscript, all authors had complete access to the study's data.

2.2 Clinical and laboratory parameters

Patients underwent detailed clinical assessments, including anthropometry (e.g., BMI and waist circumference) and abdominal ultrasound. Blood tests, including CBC, liver function tests, lipid profile, and HbA1c, were performed in the month preceding the LSM and CAP measurements.

The diagnosis of hypertension and diabetes was done according to established protocols [13, 14]. Metabolic syndrome was defined according to the American Heart Association criteria and the National Heart, Lung, and Blood Institute [15.[

2.3 Transient Elastography (Fibroscan)

Experienced operators assessed LSM and CAP with a FibroScan (echosens-France) 502 M probe. The patients were asked to fast three hours before the examination. To be considered valid, measurements had to be taken ten times with an accuracy of 60% or higher and an interquartile range of less than 30%. CAP, which is measured in decibels per meter, is a mean estimation of the attenuation of ultrasound at 3•5 MHz. The unit of measurement for LSM is Kilopascals (kPa). In patients with a BMI of less than or equal to 30 kg/m2, measures were taken using the M probe while in patients with BMI 30 kg/m2 or more, measures were taken using the XL probe [16]. Significant fibrosis ≥ F2 was determined as LSM ≥8 kPa. The Controlled

Attenuation Parameter (CAP) thresholds was used for grading steatosis are as follows:

- S1 (Mild steatosis): CAP values between 288 and 302 dB/m
- S2 (Moderate steatosis): CAP values between 302 and 355 dB/m
- S3 (Severe steatosis): CAP values above 355 dB/m [16, 17.[

2.4.Calculation of Score Values

Scores were calculated using their respective formulas:

- The FAST score was calculated using [eˆ(– 1•65 + 1•07 × In(LSM) + 2•66∗10−8 × CAP3 –63.3 × AST−1)]/[1 + eˆ(– 1•65 + 1•07 × In(LSM) + 2•66∗10−8 × CAP3 – 63.3 × AST−1)].[8[
- There is a 90% specificity rate for ruling in biopsy-proven fibrotic NASH (NAFLD with a histological NAFLD activity score [NAS] ≥4 and fibrosis ≥2) when the FAST score is ≥0.67, which is used to identify fibrotic NASH. [18[
- ABDA score = 24.74+ (3.65*ln (ALT)) +(0.14* BMI) + (1.41*Diabetes [present (1)/absent (0)]) + (0.05*Age) [11].

2.5 Statistical analysis

Statistical analysis was carried out using SPSS software version 20.0 (IBM Corp, Armonk, NY). Categorical variables were expressed as numbers and percentages, while continuous data were tested for normality using the Kolmogorov-Smirnov and Shapiro-Wilk tests. Normally distributed variables were presented as means and standard deviations, whereas non-normally distributed data were summarized using medians, minimum and maximum values. Comparisons between groups for continuous variables were made using the Student's t-test for normally distributed data, and the Mann-Whitney U test when distributions were non-normal. The chi-square test assessed associations between categorical variables, with Monte Carlo correction applied when over 20% of cells had expected counts below 5. Receiver operating characteristic (ROC) curve analysis was employed to evaluate the diagnostic accuracy of the ABDA score, including sensitivity, specificity, and the area under the curve (AUC). The optimal cutoff value was identified based on the Youden index.

RESULTS

Characteristics of participants

According to FAST score, two groups were formed. Table 1

- Group I: 124 (88.6%) without fibrotic NASH (FAST < 0.67.(
- Group II: 16 (11.4%) with fibrotic NASH (FAST ≥0.67 .(

Mean age was 48.4 ± 7.9 years, 46.4% were males, and the mean BMI in the study was 35.6 ± 6.8. Diabetes, hypertension and metabolic syndrome were present in 77 (55.0%), 59 (42.1%) and 97 (69.3%) subjects, respectively. Age and waist circumference were significantly increased among patients with fibrotic NASH (FAST score <0.67) (P<0.001), Table 2

Regarding FAST score parameters, the mean values of LSM, CAP and AST values were 6.61 ± 2.31 kPa, 302.2 ± 44.6 dB/m and 35.2 ± 20.4 IU/L, respectively. Among the 140 subjects in the studied groups, 86 (61.4%) were F0-F1, 39 (27.9%) were F2, 15 (10.7%) were F3 and there was no F4. The mean LSM, among fibrotic NASH group was 10.39 ± 2.21 kPa among them 10 (62.5%) patients with advanced fibrosis (F3)(10– <14) compared to mean of 6.12 ± 1.83 kPa , among them 84 (67.7%) patients with F0-F1 in the other group Table 2.

Table 3 showed the comparison of the selected biochemical data between the studied groups of patients showing that; ALT, AST, platelets, HDL and total cholesterol were significantly increased among patients with fibrotic NASH (FAST score <0.67) (P<0.001 .(

The ABDA score could identify 15/16 (93.75%) patients with fibrotic NASH among the participants showing significant increase in fibrotic NASH group compared to the other group (P<0.001) with mean and median of -0.32 ± 1.77 and 0.01(-4.17 – 2.04), (Table 3 .(

Diagnostic performance for ABDA score to discriminate patients with fibrotic NASH (Table 4 & FIG 1(

Diagnostic performance of ABDA score in terms of sensitivity, specificity, positive and negative predictive values is represented by cutoff value

>-2.678 and 93.75, 84.68, 44.1, 99.1 respectively.

The ABDA score had high AUROC of 0.933 [95% confidence interval (CI), 0.882 – 0.985].

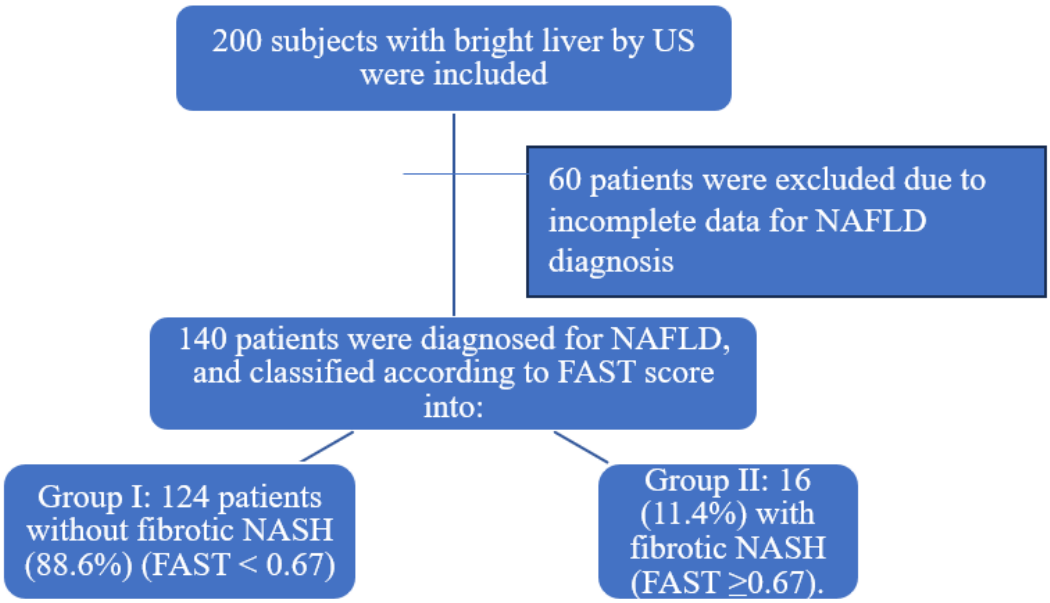

Figure (1): Flowchart for patient selection and classification using FAST score.

Table (1): Distribution of the studied Subjects according to FAST Score (n = 140)

	No. (%)
FAST Score	
Subjects without fibrotic NASH (< 0.67)	124 (88.6%)
Subjects With fibrotic NASH (≥ 0.67)	16 (11.4%)
Mean ± SD.	0.29 ± 0.23
Median (Min. – Max.)	0.22 (0.01 – 0.90)

no: number of cases, **SD:** Standard deviation

FAST: Fibro Scan-aspartate aminotransferase; NASH: non-alcoholic steatohepatitis

Table (2):Comparison between fibrotic and non-fibrotic group according to clinical, anthropometric and fibro scan parameters

	Total (n = 140)	Fast score Without fibrotic NASH (n = 124)	With fibrotic NASH (n = 16)	P
Age (years)				
Mean ± SD.	48.4 ± 7.9	47.8 ± 7.7	53.0 ± 8.0	0.012*
Median (Min. – Max.)	47.5 (21 – 70)	46 (21 – 68)	52 (40 – 70)	
Sex				
Male	65 (46.4%)	57 (46.0%)	8 (50.0%)	0.761
Female	75 (53.6%)	67 (54.0%)	8 (50.0%)	
HTN	59 (42.1%)	50 (40.3%)	9 (56.3%)	0.225
DM	77 (55.0%)	69 (55.6%)	8 (50.0%)	0.669
Metabolic syndrome	97 (69.3%)	85 (68.5%)	12 (75.0%)	FEp=0.776
Body weight (kg)				
Mean ± SD.	99.1 ± 16.9	99.4 ± 16.4	96.6 ± 20.7	0.541
Median (Min. – Max.)	98 (67 – 147)	98 (67 – 147)	93.5 (70 – 145)	
Height (cm)				
Mean ± SD.	167.4 ± 9.2	167.9 ± 9.0	163.4 ± 10.2	0.065
Median (Min. – Max.)	167 (148 – 187)	167 (150 – 187)	160 (148 – 180)	
Waist circumference (cm)				
Mean ± SD.	111.9 ± 12.7	110.9 ± 12.7	119.5 ± 10.2	0.010*
Median (Min. – Max.)	113 (80 – 140)	110 (80 – 140)	120.5 (88 – 135)	
Body mass index (kg/m^2)				
Mean ± SD.	35.6 ± 6.8	35.4 ± 6.4	36.6 ± 9.4	0.514
Median (Min. – Max.)	34.6 (24.9 –58.9)	34.6 (24.9 –58.9)	34.2 (25.1 –58.1)	
Fibroscan LSM (kPa)				
F0 –F1 (2 – 7)	86 (61.4%)	84 (67.7%)	2 (12.5%)	<0.001*
F2 (7.5 –<10)	39 (27.9%)	35 (28.2%)	4 (25.0%)	FEp=1.000
F3 (10 –<14)	15 (10.7%)	5 (4.0%)	10 (62.5%)	FEp <0.001*
Mean ± SD.	6.61 ± 2.31	6.12 ± 1.83	10.39 ± 2.21	<0.001*
Median (Min. – Max.)	6.30 (3.3 –13)	5.75 (3.3 –10.3)	10.05 (6.8 –13)	
CAP				
S1	16 (11.4%)	16 (12.9%)	0 (0%)	FEp=0.216
S2	40 (28.6%)	40 (32.3%)	0 (0%)	FEp=0.006*
S3	84 (60.0%)	68 (54.8%)	16 (100%)	0.001*
CAP (dB/m)				
Mean ± SD.	302.2 ± 44.6	295.3 ± 41.7	355.6 ± 26.6	<0.001*
Median (Min. – Max.)	302 (219 – 400)	300 (219 – 400)	360.5 (306 – 398)	

HTN: hypertension; DM: diabetes mellitus; cap: controlled attenuation parameter; kPa: kilopascal;

dB/m :decibel-milliwatts; SD: Standard deviation;t: Student t-test;χ^2: Chi square test **FE: Fisher Exact p: p** value for comparing between the two studied groups *****: Statistically significant at p ≤ 0.05

Table (3):Comparison between the two studied groups according to laboratory investigations and ABDA score

	Total (n = 140)	Fast score		P
		Without fibrotic NASH (n = 124)	With fibrotic NASH (n = 16)	
ALT (U/L)				
Mean ± SD.	36.2 ± 22.9	30.4 ± 13.9	80.9 ± 29.5	<0.001*
Median (Min. – Max.)	32 (13 – 143)	28 (13 – 77)	75.7 (35 – 143)	
AST (U/L)				
Mean ± SD.	35.2 ± 20.4	30.1 ± 13.4	75.5 ± 20.2	<0.001*
Median (Min. – Max.)	31.5 (11 – 110)	28 (11 – 72)	72 (32 – 110)	
Albumin (g/dL)				
Mean ± SD.	4.2 ± 0.5	4.2 ± 0.5	4.2 ± 0.7	0.777
Median (Min. – Max.)	4.1 (3.2 – 5.9)	4.1 (3.2 – 5.9)	4.1 (3.2 – 5.8)	
PLT(x10^3/cmm)				
Mean ± SD.	220.7 ± 42.4	225.6 ± 39.6	182.3 ± 44.8	<0.001*
Median (Min. – Max.)	228.5 (95 – 344)	230 (153 – 344)	180 (95 – 248)	
Triglyceride (mg/dl)				
Mean ± SD.	184.0 ± 43.3	183.6 ± 44.3	187.4 ± 35.6	0.564
Median (Min. – Max.)	190 (45 – 320)	188.5 (45 – 320)	195 (115 – 253)	
Total Cholesterol (mg/dl)				
Mean ± SD.	214.3 ± 31.7	212.6 ± 32.7	227.1 ± 18.8	0.014*
Median (Min. – Max.)	224 (118 –257.3)	223.5(118 –257.3)	233 (189 – 249)	
HDL (mg/dl)				
Mean ± SD.	44.2 ± 7.8	44.7 ± 7.7	40.5 ± 8	0.035*
Median (Min. – Max.)	46 (25 – 55)	47 (25 – 55)	37.8 (28 – 51)	
ABDA Score				
Mean ± SD.	-3.95 ± 2.29	-4.42 ± 1.90	-0.32 ± 1.77	<0.001*
Median (Min. – Max.)	-4.48(-8.88 –2.04)	-4.65(-8.88 –1.91)	0.01(-4.17 –2.04)	

SD: Standard deviation **t: Student t-test** **U: Mann Whitney test**

χ^2: Chi square test **MC: Monte Carlo**

p: p value for comparing between the two studied groups ***:** Statistically significant at $p \leq 0.05$

ALT: alanine aminotransferase ; AST: aspartate aminotransferase ; PLT: platelets ; HDL: high-density lipoprotein cholesterol ;

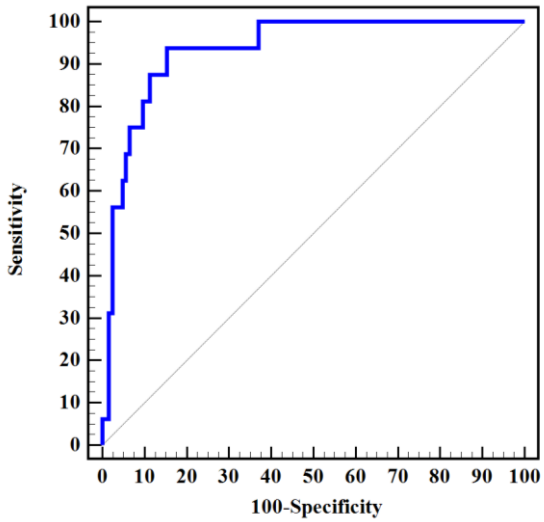

Figure (1):ROC curve for ABDA to discriminate patients with fibrotic NASH (n = 16) from patients without fibrotic NASH (n = 124)

Table (4):Diagnostic performance for ABDA score to discriminate patients with fibrotic NASH (n = 16) from patients without fibrotic NASH (n = 124)

	AUC	p	95% C.I	Cut off	Sensitivity	Specificity	PPV	NPV
ABDA Score	0.933	<0.001*	0.882 –0.985	>-2.678#	93.75	84.68	44.1	99.1

AUC: Area under a Curve; p value: Probability value CI: Confidence Intervals
NPV: Negative predictive value PPV: Positive predictive value
*: Statistically significant at p ≤ 0.05 #Cut off was selected according to Youden index

DISCUSSION

MAFLD is a new terminology introduced recently with the aim of picking up more fatty liver disease patients at high risk of adverse metabolic and cardiovascular consequences. Recently there is great body of evidence concerned with understanding the underlying etiologies and possibility of early diagnosis and early lifestyle modification.

Without doing liver biopsies, it is difficult to evaluate the actual prevalence of fibrotic NASH within the community, particularly in asymptomatic individuals; hence the need for alternative non-invasive, dependable diagnostic tests were required. Among these intriguing new scores, one that showed promise for predicting fibrotic NASH was the ABDA score, which combines ALT, BMI, diabetes, and age (11.(

The goal of current noninvasive clinical scoring is to identify advanced fibrosis, the most significant predictor of death in NAFLD. However, a key factor contributing to liver damage is the degree of hepatic inflammation. In this case, it has been determined that having NASH with marked activity (NAS ≥4) is a prerequisite for joining NAFLD clinical studies. This is primarily caused by (1) people with active disease having a higher histological response to medication therapy and (2) including

people with fibrotic NASH increases the likelihood that the estimated number of clinical events will take place during the study observation period. [6, 7 [

To identify fibrotic NASH, three noninvasive scores have been developed: the transient elastography-based FAST score (AST, CAP, LSM), and two blood-based scores, MACK-312 (AST, glucose, insulin, cytokeratin 18) and NIS413 (miR-34a-5p, alpha-2 macroglobulin, YKL-40, HbA1c). [8-10] ABDA score was recently introduced based on ALT, BMI, diabetes, and age to identify patients with fibrotic NASH.[11] Our objective was based on the study of the ABDA score in determining if NAFLD individuals had fibrotic NASH .

According to our study increasing age was a risk factor for fibrotic NASH also, increased waist circumference was associated with progression to fibrotic NASH. On the contrary, the presence of HTN, DM or metabolic syndrome doesn't correlate with fibrotic NASH. This spots the light that metabolic syndrome components are essential for defining MAFLD, but not necessarily a causal relation for fibrosis progression, meanwhile there was a non-significant tendency toward higher BMI values as fibrosis stages progressed (P=0.514; table 2). On the other hand, several studies have failed to find a correlation between obesity, diabetes, and progressive fibrosis. [19] Moreover, study's findings, which indicate that NASH screening does not yield a cost-effective outcome for people with diabetes. [20[

Most of the Egyptian population consists of young adults, and the country ranks among the top 10 in terms of obesity prevalence. However, if NAFLD is prevalent among this demographic, it could pose a serious threat to public health and place a heavy strain on healthcare systems in the area. [21[

Patients with fibrotic NASH had substantially higher transient elastography values, which varied from 3.3 to 13 kPa. Thirty-four participants, or 38.6%, exhibited transient elastography values consistent with F2-F3 fibrosis; 39 of these individuals exhibited F2 fibrosis (≥7.5 kPa), and 15 exhibited F3 fibrosis (≥ 10 kPa). F4 fibrosis (≥14kPa) was not observed in any volunteers. The correlation between rising fibrosis stages and numerically higher CAP score values was also shown to be statistically significant ($p < 0.001$; table 2). In NAFLD patients who underwent liver biopsy, CichoŽ-Lach et al. found a significant relationship between fibrosis stage and liver stiffness measurements. The findings of transient elastography (Fibroscan) corroborate this conclusion. [22.[

ABDA score was originally developed in the study done by Anand, et al. to detect fibrotic NASH in the derivation cohort and revealed a specificity and sensitivity of 88.3% and 88.9%, respectively, for an ABDA score of ≥ –3.52 [11]. With a sensitivity of 93.75% and a specificity of 84.6 %, the current study found that fibrotic NASH could be detected in the Egyptian cohort using an ABDA score at a cutoff of >-2.67 ..

According to the study, the ABDA score is based on standard anthropometric and blood test parameters. We found that the ABDA score showed an excellent sensitivity and specificity of approximately 90%. in predicting fibrotic NASH . It can identify fibrotic NASH and significantly decrease the frequency of liver biopsies in patients with NAFLD .

Limitations of the study included that it was a single-center study on a relatively small number. No liver biopsy was taken to confirm the results of the FAST score. More large-cohort studies evaluating the applicability of the ABDA score alone or in combination with other non-invasive scores targeting fibrotic NASH are needed to generalize the data from this study.

CONCLUSION

Anthropometric and laboratory characteristics that are readily available are necessary for the blood-based ABDA score. It provides a feasible, precise, and non-invasive approach to diagnose fibrotic NASH, with a good sensitivity and specificity. In addition to reducing the need for liver biopsies in NAFLD patients, it can detect fibrotic NASH.

LIST OF ABBREVIATIONS

NAFLD: Non-alcoholic fatty liver disease

NASH: Non-alcoholic steatohepatitis

MAFLD: metabolic-associated fatty liver disease

AASL: American Association for the Study of Liver

EASLD: European Association for the Study of the Liver diseases

FAST score: FibroScan-aspartate aminotransferase

NIS4 :(miR-34a-5p, alpha-2 macroglobulin, YKL-40, and glycated haemoglobin)

MACK-3:(hoMa, Ast, CK18)

CAP: controlled attenuation parameter

LSM: liver stiffness measurement

AST :aspartate aminotransferase

AACE;American Association of Clinical Endocrinology

BMI:body mass index

ROC:receiver operating characteristic curve

AUC: area under the curve

PPV:positive predictive value

NPV:negative predictive value

Ethical considerations:

Study was approved from the Tanta University Faculty of Medicine Ethical Committee (Approval Number: 36264PR491/1/24). Each participant's signed informed consent was acquired.

Author contribution: We declare that all listed authors have made substantial contributions to all of the following three parts of the manuscript:

-Research design, or acquisition, analysis or interpretation of data؛

-drafting the paper or revising it critically؛

-approving the submitted version.

We also declare that no-one who qualifies for authorship has been excluded from the list of authors.

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Conflict of interest

None

HIGHLIGHTS

- Fibrotic nonalcoholic steatohepatitis (NASH) , defined as NASH, NAFLD activity score ≥4, and fibrosis stage ≥2, is a high risk for cirrhosis.
- Noninvasive evaluation of the histological characteristics of nonalcoholic fatty liver disease (NAFLD) has been a focus of intense investigation.
- ABDA score was recently developed for non invasive identification of fibrotic NASH

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