Med. J. Cairo Univ., Vol. 93, No. 1, Accepted 23/2/2024
DOI: 10.22608/MJCU. 357-367, March 2025
www.medicaljournalofcairouniversity.net

Non-Alcoholic Fatty Liver Disease in Diabetes Mellitus Patients on Regular Hemodialysis

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Abstract

Background: Since MAFLD and CKD, especially diabetic nephropathy, are two very prevalent entities with important consequences for cardiovascular health. They share common and complex risk factors and pathophysiological pathways, and also MAFLD can precede CKD. Moreover, when they coexist, their deleterious effects are potentiated, so It's important to follow up kidney functions in fatty liver disease and also to follow up fatty liver in renal patients even if reach End stage.

Aim of Study: Detection of degree of risk of liver fibrosis in ESRD on RHD who complicated with metabolic syndrome and fatty liver to prevent progression of this fibrosis to cirrhosis and decrease incidence of Decompensated liver disease and HCC in this type of patients.

Patients and Methods: A group of 50 ESRD patients who are on regular hemodialysis (3 times / week) will be enrolled to the study, study will be performed in the Renal dialysis unit, Souad Kafafi Teaching Hospital, Faculty of Medicine, MUST University. The study will span a period of six months, involving a detailed analysis of patient data to achieve the research objectives.

Results: An overwhelming majority, 94% (47 patients), showed that they had fatty liver. The liver enzymes AST (22.43±10.86) and ALT (19.71±11.0) show relatively low averages with ranges extending from 6 to 48 and 6 to 53, respectively, suggesting mild liver enzyme elevation in some cases but mostly within normal limits. Albumin levels have a mean of 3.18g/dL (±0.58), with a range from 1.9 to 4.6, reflecting generally low and low normal levels in most patients. The FIB-4 score, a non-invasive index used to assess liver fibrosis, for a cohort of patients. The mean FIB-4 score is 1.25 (±0.56), with a range from 0.44 to 2.72, suggesting varying degrees of fibrosis risk among the patients. Notably, 68% (34 patients) are classified as low risk, while 32% (16 patients) fall into the intermediate risk category. Importantly, one patient is categorized as high risk. The mean NAFLD score is –0.37±1.29, with a wide range from –3.08 to 1.89, reflecting varying degrees of liver fibrosis severity. Notably, 22% of patients fall into the F0F2 category, indicating no significant fibrosis. A majority, 60%, fall into the "Undetermined" range, suggesting that further diagnostic evaluation, such as a liver biopsy, might be necessary to assess their fibrosis status accurately. Meanwhile, 22% of patients exhibit significant fibrosis, categorized as F3-F4.

Conclusion: The prevalence of NAFLD in diabetic patients on RHD was high. NAFLD can be diagnosed with ultrasonography. The FIB-4 score has demonstrated limited utility in this specific patient population, whereas the NAFLD Fibrosis Score (NFS) exhibits only a moderate capacity to predict advanced hepatic fibrosis. Despite its suboptimal diagnostic accuracy, the NFS may serve as a pragmatic alternative in clinical scenarios where advanced diagnostic modalities, such as transient elastography (TE) or magnetic resonance imaging (MRI), are either unavailable or inaccessible. This underscores the need for careful consideration of diagnostic tools in resource constrained settings to optimize patient management.

Key Words: *NAFLD – Diabetic patients – RHD – FIB4 score – NAFLD Fibrosis score.*

Introduction

Metabolic dysfunction-associated steatotic liver disease (MASLD) is the most common cause of chronic liver disease worldwide, affecting up to ~30% of the general adult population **[1]**. MASLD includes a spectrum of progressive liver conditions spanning from simple hepatic steatosis to steatohepatitis, advanced fibrosis, and cirrhosis **[2]**.

MASLD is strongly associated with greater insulin resistance, increased adiposity, and type 2 diabetes mellitus (T2DM), which may contribute to an increased risk of developing adverse hepatic and extra-hepatic clinical outcomes **[3]**.

MASLD is considered as a multisystem disease that is associated with an increased risk of developing chronic kidney disease (CKD) **[4]**, cardiovascular disease (CVD) **[5]** T2DM **[6]**.

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CKD is a major public health problem (affecting up to nearly 15% of the general adult population), and its global incidence is expected to further increase in the future. CKD is an established risk factor for CVD, and all CKD stages are associated with an increased risk of CVD events and mortality.

Moreover, as CKD develops, it can lead to end-stage kidney disease requiring renal replacement therapy, and result in premature death **[7].**

Since MAFLD and CKD, especially diabetic nephropathy, are two very prevalent entities with important consequences for cardiovascular health. They share common and complex risk factors and pathophysiological pathways, and also MAFLD can precede CKD.

Moreover, when they coexist, their deleterious effects are potentiated, so It's important to follow-up kidney functions in fatty liver disease and also to follow-up fatty liver in renal patients even if reach End stage.

Aim of the study:

Detection of degree of risk of liver fibrosis in ESRD on RHD who complicated with metabolic syndrome and fatty liver to prevent progression of this fibrosis to cirrhosis and decrease incidence of Decompensated liver disease and HCC in this type of patients.

Patients and Methods

Study setting:

This study was conducted in the Renal dialysis unit, Souad Kafafi Teaching Hospital, Faculty of Medicine, MUST University during 2023 Study population:

A group of 50 ESRD patients who are on regular hemodialysis (3 times / week) will be enrolled to the study.

Design:

This study is a cross-sectional study involving diabetic patients with End Stage Renal Disease ESRD attending the hemodialysis unit for a period of 3 months.

Ethical consideration:

The Faculty of Medicine Research Ethics Committee (REC) FWA 00025577 of Must University granted ethical approval for the present investigation design. The Declaration of Helsinki, the World Medical Association's code of ethics for investigations human related, guided the conduct of this research. An informed consent will be obtained from all participants in the study.

Inclusion criteria:

End stage on regular hemodialysis, diabetic, hypertensive, dyslipedimic, Obese and overweight

Exclusion criteria:

Patients who refused to participate in the study, patients on RHD due to causes other than diabetes mellitus, patients with history of liver disease, patients with history of malignancy.

Methods: All patients are subjected to the following:

1- Gathering full medical history, examination, etiology and duration of ESRD, and other comorbidities.
2- Abdominal ultrasound.
3- Laboratory investigations (AST-ALT-platelets) to detect FIB4 score.
4- Anthropometric measures with age, BMI, laboratory investigation (albumin) to detect NAFLD fibrosis score.

Statistical analysis:

Recorded data were analyzed using the statistical package for social sciences, version 23.0 (SPSS Inc., Chicago, Illinois, USA). The quantitative data were presented as mean ± standard deviation and ranges when their distribution was parametric (normal) while nonnormally distributed variables (non-parametric data) were presented as median with interquartile range (IQR). Also, qualitative variables were presented as number and percentages. Data were explored for normality using Kolmogorov-Smirnov and Shapiro-Wilk Test.

The following tests were done:

- Independent-samples *t*-test of significance was used when comparing between two means.
- The Comparison between groups with qualitative data was done by using.

Chi-square test:

- The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the *p*-value was considered significant as the following:
  - Probability (*p*-value).
  - *p*-value <0.05 was considered significant.
  - *p*-value <0.01 was considered as highly significant.
  - *p*-value >0.05 was considered insignificant.

Results

The provided data summarizes the demographic characteristics of a group of 50 patients.

The mean age of the patients is 60.45 years, with a standard deviation of 11.11 years, indicating a moderate spread in the ages. The age range spans from 35 to 86 years, showing a diverse representation of adult and elderly patients.

In terms of gender distribution, the group is balanced, with 48% male (24 patients) and 52% female (26 patients), which suggests an almost equal representation of both genders in the study population

Table (1): Demographic characteristics of studied patients.

	Studied patients (n=50)	
	N	%
Age (year):		
Mean ± SD	60.45±11.11	
Range	35-86	
Gender:		
Male	24	48.0
Female	26	52.0

Table (2): BMI and comorbidities of studied patients.

	Studied patients (n=50)	
	N	%
BMI (Kg/m^2):		
Mean ± SD	28.89±3.41	
Range	25.1-41.1	
Diabetic:		
Positive	50	100
Negative	0	0
Hypertension:		
Positive	50	100
Negative	0	0
BMI category:		
Underweight	0	0
Normal weight	0	0
Overweight	39	78.0
Obese	11	22.0

This data provides insight into the BMI, diabetes status, and hypertension prevalence among a group of 50 patients. The mean BMI is 28.89 kg/m^2, with a standard deviation of 3.41, ranging from 25.1 to 41.1 kg/m^2, indicating that all patients fall within overweight or obese categories.

Specifically, 78% of the patients are classified as overweight, while 22% are categorized as obese. Additionally, all patients in this cohort are diabetic. Hypertension is another prevalent comorbidity, with 100% of the patients being hypertensive.

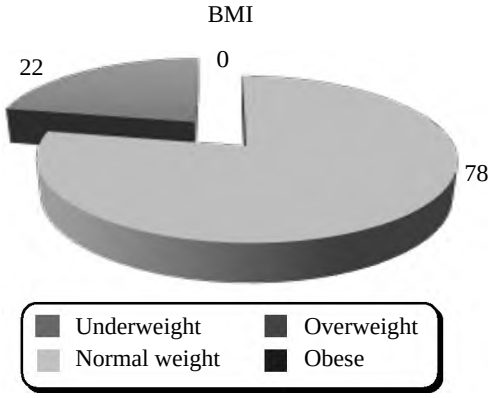


Fig. (1): BMI Category among the studied patients.

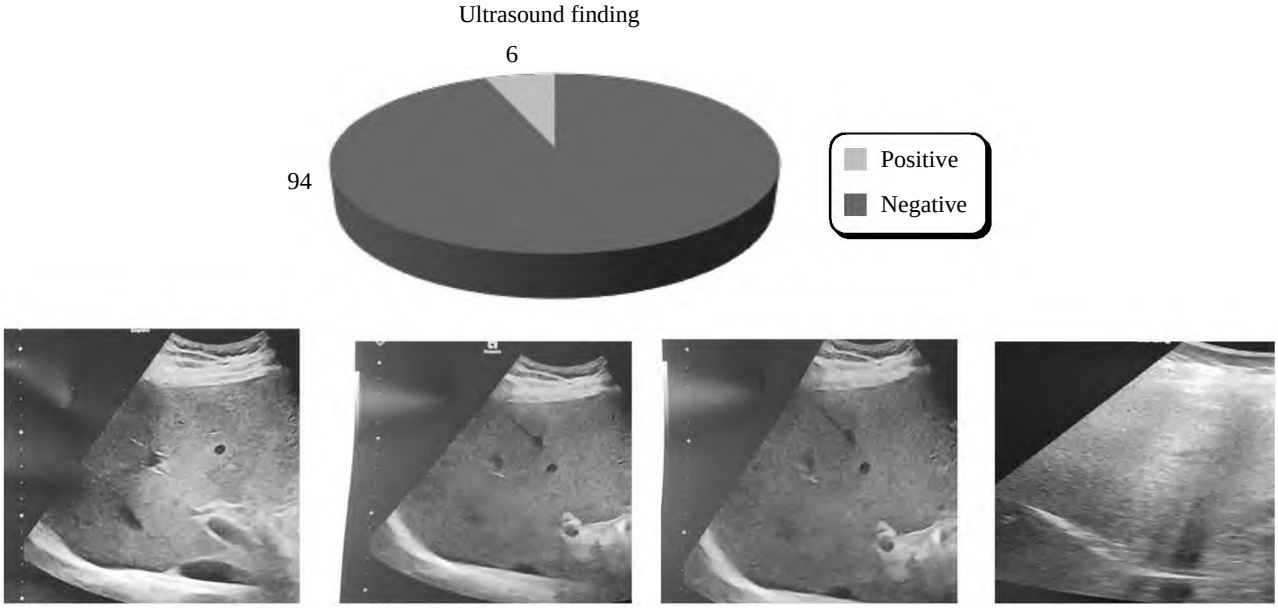
Table (3): Ultrasound findings of studied patients.

	Studied patients (n=50)	
	N	%
Ultrasound:		
Fatty liver	47	94.0
Normal liver	3	6.0

This data illustrates the prevalence of positive ultrasound findings of fatty liver among a cohort of 50 patients. An overwhelming majority, 94% (47 patients), showed that they had fatty liver (68% of them had grade 2 to 3 steatosis), while only 6% (3 patients) had normal liver.

Classification: (B-mode ultrasound) (Ferraioli & Monteiro) [8]:

- Grade I: Diffusely increased hepatic echogenicity but periportal and diaphragmatic echogenicity is still appreciable.
- Grade II: Diffusely increased hepatic echogenicity obscuring periportal echogenicity but diaphragmatic echogenicity is still appreciable.
- Grade III: Diffusely increased hepatic echogenicity obscuring periportal as well as diaphragmatic echogenicity.



(A, B, C): Grade II Steatosis. (D): Grade III Steatosis.

Fig. (2): Ultrasound finding among the studied patients.

Table (4): Hematological and biochemical parameters of studied patients.

	Studied patients (n=50)	
	N	%
Platelets:		
Mean ± SD	259.25±84.33	
Range	111-478	
AST:		
Mean ± SD	22.43±10.86	
Range	6-48	
ALT:		
Mean ± SD	19.71±11.0	
Range	6-53	
Albumin:		
Mean ± SD	3.18±0.58	
Range	1.9-4.6	

Table (5): Lipid profile of studied patients.

	Studied patients (n=50)	
	N	%
Cholesterol:		
Mean ± SD	165.25±51.67	
Range	56-250	
TG:		
Mean ± SD	198.35±97.73	
Range	59-420	
LDL:		
Mean ± SD	83.35±38.55	
Range	15-169	
HDL:		
Mean ± SD	41.89±17.92	
Range	20-131	

This data highlights key hematological and biochemical markers for a cohort of patients.

The mean platelet count is 259.25 (±84.33), with values ranging from 111 to 478, indicating variability within normal and potentially elevated ranges. The liver enzymes AST (22.43±10.86) and ALT (19.71±11.0) show relatively low averages, with ranges extending from 6 to 48 and 6 to 53, respectively, suggesting mild liver enzyme elevation in some cases but mostly within normal limits. Albumin levels have a mean of 3.18 g/dL (±0.58), with a range from 1.9 to 4.6, reflecting generally low and low normal level in most patients.

This data provides an overview of the lipid profile for studied patients.

The mean cholesterol level is 165.25mg/dL (±51.67), with a range from 56 to 250mg/dL, reflecting a broad distribution from potentially low to elevated cholesterol levels.

Triglycerides (TG) have a higher mean of 198.35mg/dL (±97.73) with a wide range of 59 to 420mg/dL, indicating that a significant portion of the patients may have elevated triglycerides, a common risk factor for cardiovascular disease. The LDL (bad cholesterol) mean is 83.35mg/dL (±38.55), ranging from 15 to 169mg/dL, with values falling

within both normal and elevated ranges. HDL (good cholesterol) shows a lower mean of 41.89mg/dL (±17.92), ranging from 20 to 131mg/dL, which may indicate that many patients have suboptimal HDL levels.

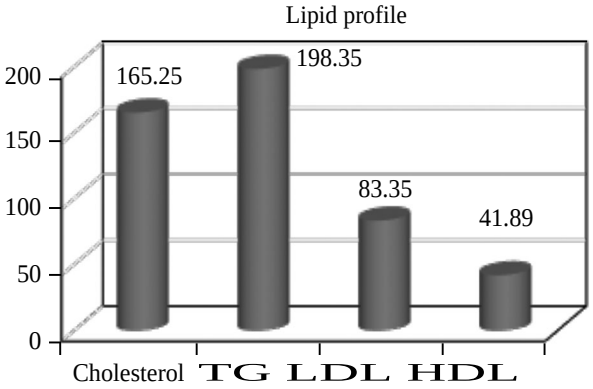


Fig. (3): Lipid Profile among the studied patients.

Table (6): FIB-4 Score distribution and risk assessment of studied patients.

	Studied patients (n=50)	
	N	%
FIB 4 score:		
Mean ± SD	1.25±0.56	
Range	0.44-2.72	
FIB 4 category:		
Low risk (≤1.3)	34	68.0
Intermediate risk (1.31-2.7)	15	30.0
High risk (>2.67)	1	2.0

This data presents the FIB-4 score, a non-invasive index used to assess risk of liver fibrosis, for a cohort of patients. The mean FIB-4 score is 1.25 (±0.56), with a range from 0.44 to 2.72, suggesting varying degrees of fibrosis risk among the patients. Notably, 68% (34 patients) are classified as low risk, while 32% (16 patients) fall into the intermediate risk category. Importantly, one patient is categorized as high risk.

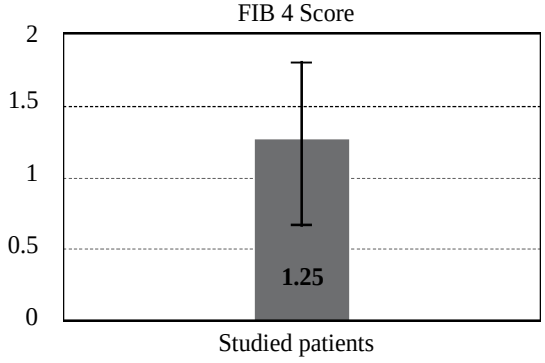


Fig. (4): FIB-4 Score among the studied patients.

Table (7): NAFLD Score distribution among studied patients.

	Studied patients (n=50)	
	N	%
NAFLD score:		
Mean ± SD	–0.37±1.29	
Range	–3.08-1.89	
NAFLD category:		
F0-F2 (<-1.455)	11	22.0
Undetermined (-1.455-0.676)	30	60.0
F3-F4 (>0.676)	9	18.0

The table presents the distribution of NAFLD scores among studied patients, providing insight into the probability of fibrosis.

The mean NAFLD score is –0.37±1.29, with a wide range from –3.08 to 1.89, reflecting varying degrees of liver fibrosis severity. Notably, 22% of patients fall into the F0-F2 category, indicating no significant fibrosis.

A majority, 60%, fall into the "Undetermined" range, suggesting that further diagnostic evaluation, such as a liver biopsy, might be necessary to assess their fibrosis status accurately. Meanwhile, 18% of patients exhibit significant fibrosis, categorized as F3-F4.

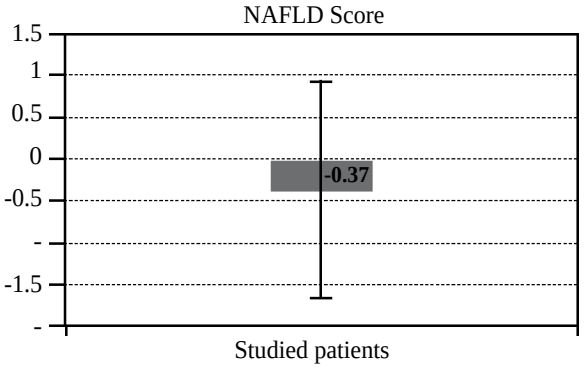


Fig. (5): NAFLD fibrosis score among the studied patients.

Table (8): NAFLD score and fib-4 score in relation to ultrasound finding among studied patients.

	Ultrasound				Test value	*p*-value
	Negative (n=3)		Positive (n=47)			
	N	%	N	%		
FIB 4 score:						
Mean ± SD	1.05±0.31		1.26±0.57		0.632	0.530
Range	0.85 – 1.41		0.44 – 2.72			
NAFLD score:						
Mean ± SD	-1.81±0.29		-0.28±1.27		2.062	0.044*
Range	-.04 – -1.48		-3.08 – 1.89			

Using: *t*-test, *p*-value >0.05 is insignificant.
**p*-value <0.05 is significant. ***p*-value <0.01 is highly significant.

The table compares Fib-4 and NAFLD scores between patients with negative (n=3) and positive (n=47) ultrasound Finding.

While the Fib-4 score showed no significant difference (p=0.530), with a mean score of 1.05 in the negative group and 1.26 in the positive group, the NAFLD score exhibited a statistically significant difference (p=0.044).

Patients with positive ultrasound results had a higher mean NAFLD score (–0.28) compared to the negative group (–1.81). This finding suggests that the NAFLD score, which reflects the likelihood of fibrosis, is strongly associated with positive ultrasound outcomes. The significance of the NAFLD score highlights its potential utility in screening for fatty liver disease, where a higher score correlates with positive ultrasound detection.

Table (9): Correlation between NAFLD Score, FIB-4 Score, and ultrasound findings.

	Ultrasound
FIB 4 score:	
r	0.090
p-value	0.530
NAFLD score:	
r	0.283
p-value	0.044*

Using: *r*: Spearman correlation coefficient.

p-value >0.05 is insignificant.

**p*-value <0.05 is significant.

***p*-value <0.01 is highly significant.

The table presents the correlation between FIB-4 and NAFLD scores with ultrasound findings for fatty liver disease.

The FIB-4 score, typically used to assess liver fibrosis, shows a weak and insignificant correlation with ultrasound results (r=0.090, p=0.530). This suggests that FIB-4 may not be a strong indicator for risk of fibrosis in patients with moderate to severe steatosis that appear on ultrasound.

In contrast, the NAFLD score exhibits a moderate positive correlation (r=0.283) with a significant p-value (0.044). This indicates that as the likelihood of increase grading of steatosis in ultrasound also the NAFLD score increases. The significant correlation underscores the NAFLD score's utility in predicting probability of risk of liver fibrosis, making it a more effective tool in this context compared to the FIB-4 score.

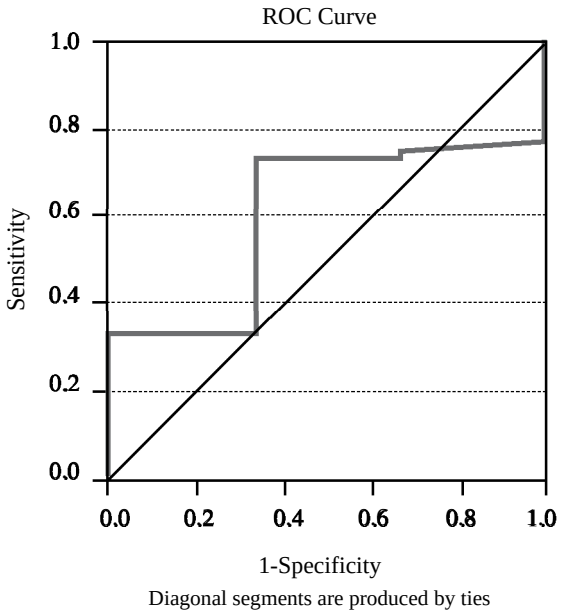


Fig. (6): ROC curve based on the relationship between the Ultrasound and the FIB-4 Score.

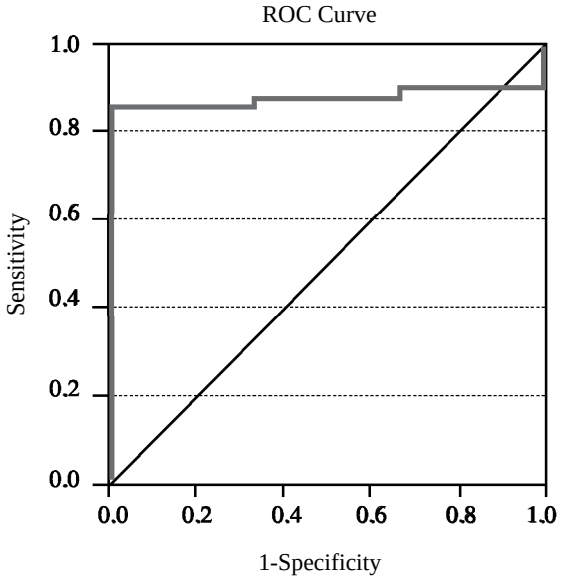


Fig. (7): ROC curve based on the relationship between the Ultrasound and the NAFLD Score.

Discussion

In this study we aimed to detect risk and degree of liver fibrosis in patients on dialysis due to diabetic nephropathy and complicated with fatty liver to prevent progression of this fibrosis to cirrhosis and decrease incidence of HCC (hepatocellular carcinoma) and other complications like cardiovascular complications in this type of patients.

This cross-sectional study was conducted on a group of 50 ESRD patients due to diabetic Nephropathy who are on regular hemodialysis (3 times

/ week) at Renal dialysis unit, Souad Kafafi University Hospital.

This was done by detecting fatty liver using ultrasound which was performed when the patient presented for hemodialysis session or if was hospitalized for other reasons and for detecting the risk and degree of liver fibrosis, we used non-invasive tests such as FIB4 score and NAFLD fibrosis Score.

The current study revealed that the mean age of studied cases is 60.45 years, with a standard deviation of 11.11 years, indicating a moderate spread in the ages. The age range spans from 35 to 86 years, showing a diverse representation of adult and elderly patients.

In terms of gender distribution, the group is fairly balanced, with 48% male (24 patients) and 52% female (26 patients), which suggests an almost equal representation of both genders in the study population.

According to Wong et al., *[9]* who aimed to study metabolic dysfunction associated fatty liver disease (MAFLD) and advanced liver fibrosis among hemodialysis patients the mean age was 59, 55% were males and 45% were females.

Mikolasevic et al. *[10]* conducted a cohort study that enrolled 62 patients of chronic kidney disease with fatty liver and revealed that the average age is 64.9±8.6 years. Most of the subjects enrolled were males.

NAFLD has the highest prevalence among males aged 40-49 and among females aged between 60 and 69. Studies show that, men are more likely to develop NAFLD compared to women of reproductive age, and the difference in prevalence tends to equalize after menopause *[11]*.

The mean BMI (Body mass index) in our study is 28.89kg/m^2, with a standard deviation of 3.41, ranging from 25.1 to 41.1kg/m^2, indicating that all patients fall within overweight or obese categories to be an entity of metabolic syndrome so other categories are excluded from the study.

Additionally, all patients in this cohort are diabetic; Hypertension is another prevalent comorbidity, with 100% of the patients being hypertensive.

A retrospective cohort study designed to describe the presence of hepatic fibrosis and steatosis in patients who had ESRD. Patients were overweight with BMI of 28.9±5.4kg/m^2 with 36% of the population obese with BMI ≥30kg/m^2, Metabolic syndrome comorbidities were common with HTN the most prevalent (96%) followed by DM (47%) *[12]*.

Sapmaz et al. *[13]* found that NAFLD was strongly associated with central obesity and significantly higher BMI values.

Our study revealed that, Majority of the patients (94%) had fatty liver, however only 6% of the cases had normal liver.

NAFLD in patients undergoing hemodialysis (HD) has a high prevalence ranging from 50.5% to 86% depending on the method used for diagnosis *[14]*.

Our study revealed that the number of diagnoses of NAFLD made by using usual ultrasound. For the diagnosis we used the following ultrasound features: Increased hepatorenal echogenicity, vascular blurring of the hepatic or portal vein and bright hepatic echo.

Yen et al. *[15]* suggest the use of CAP (controlled attenuation parameter) combined with ultrasound to screen for NAFLD in hemodialysis patients as the number of diagnoses of NAFLD in his study made by using CAP combined with ultrasound was more than 2 times the number made with ultrasound alone in the hemodialysis patients.

The case series of Stoica et al., *[14]* which addresses cardiovascular and mortality risk as a result of NAFLD in diabetes mellitus patients on chronic hemodialysis revealed that 69.2% of patients were diagnosed as NAFLD using ultrasound.

In our study The liver enzymes AST was (22.43 ±10.86) and ALT (19.71±11.0) show relatively low averages, with ranges extending from 6 to 48 and 6 to 53, respectively, suggesting mild liver enzyme elevation in some cases but mostly within normal limits. This disagreed with Behairy et al. *[16]* who revealed that ALT & AST significantly correlated with CAP of liver steatosis degree in HD patients.

BUT agreed with the studies that have shown that AST and ALT serum levels were decreased in CKD patients undergoing HD. It was hypothesized that this reduction could be caused by factors such as the withdrawal of aminotransferases during the HD session; the high lactate serum levels, which, during biochemical dosages, would rapidly consume Nicotinamide Adenine Dinucleotide Phosphate (NADPH) and result in low levels of aminotransferases; the presence of uremic factors that would inhibit the activity of these enzymes; and, finally, the deficiency of pyridoxine, a cofactor for the synthesis of the aminotransferases *[17]*.

ESRD patients, particularly those with diabetes, have significantly altered liver enzyme profiles than the general population. These results may change our view of liver enzymes levels in ESRD patients particularly ESRD patients with diabetes in routine monthly follow-up and in other occasions [18].

In our study the lipid profile showed that The mean cholesterol level is 165.25mg/dL (±51.67), with a range from 56 to 250mg/dL, Triglycerides (TG) have a higher mean of 198.35mg/dL (±97.73) with a wide range of 59 to 420mg/dL, indicating that a significant portion of the patients may have elevated triglycerides, a common risk factor for cardiovascular disease. The LDL (bad cholesterol) mean is 83.35mg/dL (±38.55), ranging from 15 to 169mg/dL, with values falling within both normal and elevated ranges. HDL (good cholesterol) shows a lower mean of 41.89mg/dL (±17.92), ranging from 20 to 131mg/dL, which may indicate that many patients have suboptimal HDL levels.of liver steatosis. This agreed with Adejumo et al. (2016) [19], who found that median serum LDLC was significantly higher, but mean serum HLC was significantly lower in CKD compared to controls. Increase BMI & hypertriglyceridemia and high LDL, low HDL defined the metabolic syndrome according to HMetS 2009 Criteria. Also, others found that metabolic syndrome was common in hemodialysis patients as a predictor of major adverse cardiovascular events [20].

Also, Julián et al. [21] reported that dyslipidemia in HD patients was due to moderately increased apoB and significantly increased apoC-III. Triglyceride-rich apoBcontaining lipoproteins (VLDL & IDL) were elevated by decreased activities of lipoprotein lipase and hepatic lipase in HD patients, resulting in hypertriglyceridemia.

The albumin in our studied patients has a mean of 3.18g/dL (±0.58), with a range from 1.9 to 4.6, reflecting generally low and low normal levels in most patients.

The mechanisms underlying hypoalbuminemia in patients with CKD are not fully understood, and multiple factors such as inadequate protein intake, protein synthesis disorders, excessive protein loss, inflammatory responses, and protein loss during dialysis contribute to its occurrence [22].

NAFLD/NASH is associated with overnutrition, hyperglycemia, insulin resistance, abnormality of lipid metabolism profile, which eventually resulted in chronic liver inflammation, liver fibrosis as well as atherosclerosis. Cardiovascular events occur as the result of atherosclerosis that was frequently associated with DM and obesity. This event is observed in NAFLD/NASH cases who exhibited chronic liver injury, and there is possibility of observing chronological albumin decline [23].

In our study the mean FIB-4 score is 1.25 (±0.56), with a range from 0.44 to 2.72, suggesting varying degrees of fibrosis risk among the patients.

Notably, 68% (34 patients) are classified as low risk, while 32% (16 patients) fall into the intermediate risk category. Importantly, one patient is categorized as high risk.

The mean NAFLD score is –0.37±1.29, with a wide range from –3.08 to 1.89, reflecting varying degrees of liver fibrosis severity. Notably, 22% of patients fall into the F0-F2 category, indicating no significant fibrosis.

A majority, 60%, fall into the “Undetermined” range, suggesting that further diagnostic evaluation, such as a liver biopsy, might be necessary to assess their fibrosis status accurately. Meanwhile, 22% of patients exhibit significant fibrosis categorized as F3-F4.

Despite the increased diagnostic accuracy of noninvasive tests to detect hepatic fibrosis in general population, utility in ESRD is challenging with no studies to date on the subset of possible NAFLD patients.

The major challenge is the reliance of most serum-based non-invasive tests on liver enzymes (AST and ALT) and clinical findings that may be nonspecific because of the underlying renal disease [12].

Non-invasive serum markers for assessment of liver fibrosis universally use AST and/or ALT. However, the levels of AST/ALT among uremic patients with chronic hepatitis on maintenance hemodialysis were only around one-third to corresponding general population [24].

Also Lee et al. [24] confirmed that the traditional cutoff value of APRI or FIB-4 to predict liver fibrosis in the general population cannot be applied to the hemodialysis population.

Arrayhani et al. [25] revealed that the noninvasive tests including APRI and FIB4 scores could be a suitable alternative to assess hepatic fibrosis.

The use of non-invasive markers in recent years has displaced the use of liver biopsy to determine advanced fibrosis. Positive predictive values (PPV) have been reported for the NAFLD score of 90% to

detect cases of advanced fibrosis. However, in this study, the positive and negative predictive value of the NAFLD score was 33% and 66%, respectively, which could suggest that these patients may possess unique characteristics that require validation of the scores in this subgroup before recommending its widespread use in this population ***[26]***.

Ibrahim et al. ***[27]*** conducted a study Relation of Liver Siderosis to Liver Fibrosis in Hemodialysis Patients With Severe Hyperferritinemia Secondary to High Doses of Intravenous Iron Supplementation and revealed that fib4 score might offer noninvasive tools for identifying advanced liver fibrosis in those patients.

Liver tests and biological scores are not useful for NAFLD detection in CRF patients. TE with CAP provides the opportunity of noninvasive screening for NAFLD as well as liver fibrosis in patients with CRF ***[28]***.

Pestana et al. ***[29]*** revealed that FIB-4 is simple, nonexpensive scoring systems with good accuracy to assess fibrosis in HCV-infected hemodialysis patients, mainly excluding both significant fibrosis or cirrhosis and may be an alternative to TE in the evaluation of this population.

The use of FIB-4 scores, which include AST and platelet count in predicting the presence or absence of advanced liver fibrosis, can be justified by the fact that in patients with advanced fibrosis, there is a decreased clearance of AST that is the result of increase hepatic fibrosis, reduced thrombopoietin release from hepatocytes and increased entrapment of platelets by the spleen. However, the use of heparin during hemodialysis may lead to thrombocytopenia and hence, affect the diagnostic accuracy of APRI and Fib4 scores in predicting liver fibrosis in ESRD patients ***[30]***.

Conclusion:

The prevalence of NAFLD in Diabetic patients on RHD is high.

NAFLD can be diagnosed with ultrasonography.

The FIB-4 score has demonstrated limited utility in this specific patient population, whereas the NAFLD Fibrosis Score (NFS) exhibits only a moderate capacity to predict advanced hepatic fibrosis. Despite its suboptimal diagnostic accuracy, the NFS may serve as a pragmatic alternative in clinical scenarios where advanced diagnostic modalities, such as transient elastography (TE) or magnetic resonance imaging (MRI), are either unavailable or inaccessible. This underscores the need for careful consideration of diagnostic tools in resource constrained settings to optimize patient management.

Additional research is required to verify the diagnosis of NAFLD and Fibrosis in Hemodialysis patients.

Conflict of interest: The authors declared no conflict of interest.

Sources of funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Author contribution: Authors contributed equally in the study.

References

1- ESLAM M., EL-SERAG H.B., FRANCQUE S., SARIN S.K., WEI L., BUGIANESI E. and GEORGE J.: Metabolic (dysfunction)-associated fatty liver disease in individuals of normal weight. Nature reviews Gastroenterology & Hepatology, 19 (10): 638-651, 2022.

2- RINELLA M.E., LAZARUS J.V., RATZIU V., FRANCQUE S.M., SANYAL A.J., KANWAL F. and NAFLD Nomenclature Consensus Group: A multisociety Delphi consensus statement on new fatty liver disease nomenclature. Hepatology, 78 (6): 19661986, 2023.

3- MANTOVANI A., SCORLETTI E., MOSCA A., ALISI A., BYRNE C.D. and TARGHER G.: Complications, morbidity and mortality of nonalcoholic fatty liver disease. Metabolism, 111: 154170, 2020.

4- HUH J.H., KIM J.Y., CHOI E., KIM J.S., CHANG Y. and SUNG K.C.: The fatty liver index as a predictor of incident chronic kidney disease in a 10-year prospective cohort study. PLoS One, 12 (7): e0180951, 2017.

5- SUNG K.C., YOO T.K., LEE M.Y., BYRNE C.D., ZHENG M.H. and TARGHER G.: Comparative Associations of Nonalcoholic Fatty Liver Disease and Metabolic Dysfunction–Associated Fatty Liver Disease With Coronary Artery Calcification: A Cross-Sectional and Longitudinal Cohort Study. Arteriosclerosis, Thrombosis, and Vascular Biology, 43 (3): 482-491, 2023.

6- SEO I.H., LEE H.S. and LEE Y.J.: Fatty liver index as a predictor for incident type 2 diabetes in community-dwelling adults: longitudinal findings over 12 years. Cardiovascular Diabetology, 21 (1): 209, 2022.

7- KALANTAR-ZADEH K., LI P.K., TANTISATTAMO E., KUMARASWAMI L., LIAKOPOULOS V., LUI S., ULASI I., ANDREOLI S., BALDUCCI A., DUPUIS S., HARRIS T., HRADSKY A., KNIGHT R., KUMAR S., NG M., POIDEVIN A., SAADI G., TONG A., LI P.K.T. and ULASI I.: Living Well With Kidney Disease by Patient and Care-Partner Empowerment: Kidney Health for Everyone Everywhere. American Journal of Hypertension, 34 (2): 220–225, 2021.

8- WONG W.K., CHAN W.K., GANAPATHY S.S. and LIM S.K.: Metabolic dysfunction-associated fatty liver disease (MAFLD) and advanced liver fibrosis among hemodialysis

patients in a multiethnic urban population in Malaysia. In Seminars in Dialysis, March Vol. 36, No. 2, pp. 107-116, 2023.

9- MIKOLASEVIC I., RACKI S., BUBIC I., JELIC I., STIMAC D. and ORLIC L.: Chronic kidney disease and nonalcoholic Fatty liver disease proven by transient elastography. Kidney and Blood Pressure Research, 37 (4-5): 305-310, 2013.

10- SAMY A.M., KANDEIL M.A., SABRY D., ABDELGHANY A.A. and MAHMOUD M.O.: From NAFLD to NASH: Understanding the spectrum of non-alcoholic liver diseases and their consequences. Heliyon, 2024.

11- SYED T., CHADHA N., KUMAR D., GUPTA G. and STERLING R.K.: Non-invasive assessment of liver fibrosis and steatosis in end-stage renal disease patients undergoing renal transplant evaluation. Gastroenterology Research, 14 (4): 244, 2021.

12- SAPMAZ F., UZMAN M., BASYIGIT S., OZKAN S., YAVUZ B., YENIOVA A. and NAZLIGUL Y.: Steatosis grade is the most important risk factor for development of endothelial dysfunction in NAFLD. Medicine, 95 (14): e3280, 2016.

13- STOICA R.A., TRIBUS L.C., MARIN R.I., DAVID T., PREDA C.M., BICA I.C. and SERAFINCEANU C.: Non-alcoholic fatty liver disease in diabetes mellitus patients on chronic hemodialysis – A case series addressing cardiovascular and mortality risks. Front. Clin. Diabetes Healthc, 4: 1113666, 2023.

14- YEN Y.H., CHEN J.B., CHENG B.C., CHEN J.F., CHANG K.C., TSENG P.L. and HU T.H.: Using controlled attenuation parameter combined with ultrasound to survey non-alcoholic fatty liver disease in hemodialysis patients: A prospective cohort study. PLoS One, 12 (4): e0176027, 2017.

15- BEHAIRY M.A., ZAKI M., SHARAWY A., EL S., WAHID T. and SAMIR R.: Relationship between parathyroid hormone level and hepatic steatosis degree by fibroscan among prevalent hemodialysis patients. Journal of the Egyptian Society of Parasitology, 53 (2): 199-210, 2023.

16- SETTE L.H.B.C. and DE ALMEIDA LOPES E.P.: Liver enzymes serum levels in patients with chronic kidney disease on hemodialysis: A comprehensive review. Clinics, 69 (4): 271-278, 2014.

17- ABDEL-ATTY-GADALLAH A., BAHNASY A.A., MILAD S. and TOULAN S.O.: Liver Enzymes in End Stage Renal Disease Patients Diabetic and Non-Diabetic. Does it Differ than General Population? Research Square (Research Square), 2024.

18- ADEJUMO O.A., OKAKA E.I. and OJOGWU L.I.: Lipid profile in pre-dialysis chronic kidney disease patients in southern Nigeria. Ghana Med. J., 50 (1): 44-9, 2016.

19- DELAUTRE A., CHANTREL F., DIMITROV Y., KLEIN A., IMHOFF O., MULLER C. and KRUMMEL T.: Metabolic syndrome in haemodialysis patients: Prevalence, determinants and association to cardiovascular outcomes. BMC nephrology, 21: 1-12, 2020.

20- JULIÁN M.T., PERA G., SOLDEVILA B., CABALLERÍA L., JULVE J., PUIG-JOVÉ C., MORILLAS R., TORÁN P., EXPÓSITO C., PUIG-DOMINGO M., CASTELBLANCO E., FRANCH-NADAL J., CUSI K., MAURICIO D. and ALONSO N.: Atherogenic dyslipidemia, but not hyperglycemia, is an independent factor associated with liver fibrosis in subjects with type 2 diabetes and NAFLD: A population-based study. European Journal of Endocrinology, 184 (4): 587–596, 2021.

21- WANG C.H., JIANG M.H., MA J.M., YUAN M.C., LIAO L., DUAN H.Z. and DUAN L.: Identification of independent risk factors for hypoalbuminemia in patients with CKD stages 3 and 4: The construction of a nomogram. Frontiers in Nutrition, 11: 1453240, 2024.

22- POWELL E.E., WONG V.W.S. and RINELLA M.: Non-alcoholic fatty liver disease. The Lancet, 397 (10290): 2212-2224, 2021.

23- LEE J. J., WEI Y.J., LIN M.Y., NIU S.W., HSU P.Y., HUANG J.C. and YU M.L.: The applicability of non-invasive methods for assessing liver fibrosis in hemodialysis patients with chronic hepatitis C. Plos One, 15 (11): e0242601, 2020.

24- ARRAYHANI M., SQALLI T., TAZI N., EL YOUBI R., CHAOUCH S., AQODAD N. and IBRAHIMI S.A.: Non invasive assessment of liver fibrosis in chronic hemodialysis patients with viral hepatitis C. Pan African Medical Journal, 22 (1), 2015.

25- BARRETO I.Y., FLOREZ D.R. and DAZA J.C.: Risk Factors for Liver Fibrosis in Diabetic Patients with End-stage Renal Disease. Colombian Journal of Gastroenterology, 38 (3): 278-289, 2023.

26- IBRAHIM W.H., ABOKRESHA M.M., NIGM D.A., ABDELAL S.M., KELANI A. and ALY M.G.: Relation of liver siderosis to liver fibrosis in hemodialysis patients with severe hyperferritinemia secondary to high doses of intravenous iron supplementation. Journal of Renal Nutrition, 33 (2): 337-345, 2023.

27- MIKOLASEVIC I., ORLIC L., ZAPUTOVIC L., RACKI S., CUBRANIC Z., ANIC K. and STIMAC D.: Usefulness of liver test and controlled attenuation parameter in detection of nonalcoholic fatty liver disease in patients with chronic renal failure and coronary heart disease. Wiener klinische Wochenschrift, 127: 451-458, 2015.

28- PESTANA N.F., EQUI C.M., GOMES C.P., CARDOSO A.C., ZUMACK J.P., VILLELA NOGUEIRA C.A. and PEREZ R.M.: Aminotransferase-to-platelet ratio index and Fibrosis-4 index score predict hepatic fibrosis evaluated by transient hepatic elastography in hepatitis C virus-infected hemodialysis patients. European Journal of Gastroenterology & Hepatology, 33 (1S): e260-e265, 2021.

29- WADHVA R.K., HAQUE M.M., LUCK N.H., TASNEEM A.A., ABBAS Z. and MUBARAK M.: Diagnostic accuracy of aspartate aminotransferase to platelet ratio index and fibrosis 4 scores in predicting advanced liver fibrosis in patients with end-stage renal disease and chronic viral hepatitis: Experience from Pakistan. Journal of Translational Internal Medicine, 6 (1): 38–42, 2018.

30- FERRAIOLI G. and MONTEIRO L.B.S.: Ultrasound-based techniques for the diagnosis of liver steatosis. World Journal of Gastroenterology, 25 (40): 6053–6062, 2019.

مرض الكبد الدهنى غير الكحولى لدى مرضي السكرى الذين يخضعون لغسيل الكلى بانتظام

الخلفية: نظراً لأن MAFLD، CKD، وخاصة اعتلال الكلية السكرى، هما حالتان شائعتان جداً لهما عواقب مهمة على صحة القلب والأوعية الدموية. فهما يشتركان فى عوامل خطر مشتركة ومعقدة ومسارات مرضية فيزيولوجية، كما يمكن أن يسبق MAFLD CKD. وعلاوة على ذلك، عندما يتعايشان، تزداد آثارهما الضارة، لذلك من المهم متبعة وظائف الكلى فى مرض الكبد الدهنى وكذلك متابعة الكبد الدهنى لدى مرضى الكلى حتى لو وصلوا إلى المرحلة النهائية.

الهدف من الدراسة: الكشف عن درجة خطر تليف الكبد فى ESRD على RHD الذين يعانون من متلازمة التمثيل الغذائى والكبد الدهنى لمنع تطور هذا التليف إلى تليف الكبد وتقليل حدوث مرض الكبد المعوض وسرطان الخلايا الكبدية فى هذا النوع من المرضى.

المرضى والأساليب: سيتم تسجيل مجموعة من ٥٠ ريضاً مصاباً بمرض الكلى فى مراحله النهائية والذين يخضعون لغسيل الكلى بانتظام ٣ مرات/أسبوع فى الدراسة، وستجُرى الدراسة فى وحدة غسيل الكلى بمستشفى سعاد كفافى التعليمى بكلية الطب بجامعة مصر للعلوم والتكنولوجيا. ستمتد الدراسة لمدة ستة أشهر، وتتضمن تحليلاً تفصيلياً لبيانات المرضى لتحقيق أهداف البحث.

النتائج: أظهرت الغالبية العظمى ٩٤٪، ٤٧ مريضاً أنهم مصابون بالكبد الدهنى. تظهر إنزيمات الكبد (AST)

43.22±86.10 و(ALT) 71.19±0.11 متوسطات منخفضة نسبياً مع نطاقات تمتد من إلى ٤٨ و٦ إلى ٥٣ على التوالى، مما يشير إلى ارتفاع خفيف فى إنزيمات الكبد فى بعض الحالات ولكن فى الغالب ضمن الحدود الطبيعية. متوسط مستويات الألبومين هو ١٨,٣ جم/ديسيلتر (±58.0)، مع نطاق من ٩,١ إلى ٤٦,٠، مما يعكس مستويات منخفضة ومنخفضة طبيعية بشكل عام لدى معظم المرضى.

درجة FIB-4، وهو مؤشر غير جراحى يستخدم لتقييم تليف الكبد، لمجموعة من المرضى. متوسط درجة FIB-4 هو (25.1±56.0)، مع نطاق من ٤٤,٠ إلى ٧٢,٢، مما يشير إلى درجات متفاوتة من خطر التليف بين المرضى. والجدير بالذكر أن (٦٨٪) ٣٤ مريضاً يصنفون على أنهم منخفضو الخطورة، بينما (٣٢٪) ١٦ مريضاً يقعون فى فئة الخطورة المتوسطة. والأهم من ذلك، تم تصنيف مريض واحد على أن عالى الخطورة. متوسط درجة NAFLD هو 29.1±37.0، مع نطاق واسع من -08.3 إلى 89.1، مما يعكس درجات متفاوتة من شدة تليف الكبد.

من الجدير بالذكر أن ٢٢٪ من المرضى يندرجون ضمن فئة F0-F2، مما يشير إلى عدم وجود تليف كبير. وتقع الأغلبية، ٦٠٪، ضمن نطاق غير محدد، ما يشير إلى أن التقييم التشخيصى الإضافى، مثل خزعة الكبد، قد يكون ضرورياً لتقييم حالة التليف لديهم دقة. وفى الوقت نفسه يظُهر ٢٢٪ من المرضى تليفاً كبيراً، مصنفاً ضمن فئة F3-F4.

الخلاصة: كان معدل انتشار مرض الكبد الدهنى غير الكحولى بين مرضى السكرى الذين يخضعون لغسيل الكلوى مرتفعاً. + يمكن تشخيص مرض الكبد الدهنى غير الكحولى باستخدام الموجات فوق الصوتية. وقد أظهرت درجة FIB-4 فائدة محدودة فى هذه الفئة المحددة من المرضى، فى حين أن درجة تليف الكبد الدهنى غير الكحولى (NFS) تظُهر قدرة معتدلة فقط على التنبؤ بالتليف الكبدى المتقدم. وعلى الرغم من دقتها التشخيصية غير المثالية، فقد تعمل درجة تليف الكبد الدهنى غير الكحولى كبديل عملى فى السيناريوهات السريرية حيث تكون الوسائل التشخيصية المتقدمة، مثل التصوير المرن العابر (TE) أو التصوير بالرنين المغناطيسى (MRI)، إما غير متاحة أو غير قابلة للوصول. وهذا يؤكد على الحاجة إلى دراسة متأنية لأدوات التشخيص فى البيئات ذات الموارد المحدودة لتحسين إدارة المرضى.