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Survey of non-alcoholic steatohepatitis in non-diabetic Haemodialysis patients in Beni-Suef Governorate

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Abstract:

Background: Non-alcoholic fatty liver disease (NAFLD) and chronic kidney disease (CKD) are global health issues all over the world, affecting about30% (NAFLD), and15% (CKD) of general people. Even, with absence of other risk factors such as overweight, diabetes and hypertension, there is force correlation between NAFLD and CKD. **Objective:** The target of our study is to detect the incidence of non-alcoholic steatohepatitis between non-diabetic hemodialysis patients by measuring Controlled Attenuation Parameter (CAP) using transient elastography (TE) (Fibroscan®). **Methodology:** This was a cross sectional study in Beni-Suef governorate, including **1000** hemodialysis non-diabetic ESRD patients from different hemodialysis units from all the central hospitals in Beni-Suef governorate. **Results**: According to CAP (dB/M) there were 503(50.3%) S0, 233(23.3%) S1, 100(10.0%) S1-S2, 67(6.7%) S2,10(1.0%) S2-S3 and 87(8.7%) S3. According to liver stiffness grades there were 508(50.8%) F0, 280(28.0%) F1, 57(5.7%) F2,95(9.5%) F3 and 60(6.0%) F4. There were 508(50.8%) F0 and 492(49.2%) F1:F4 with mean 6.14 (± 3.90SD) and range (2.0 – 19.90). **Conclusions:** In this study we concluded that there is a high incidence of NAFLD among non-diabetic patients on regular Hemodialysis in Beni-Suef governorate, significantly correlated with increasing degree of liver stiffness.

Keywords: NAFLD, NASH, ESRD, HD, TE

1. Introduction:

NAFLD is redundant accumulation of liver fat because of any cause except alcohol drinking [1]. NAFLD is the first cause of liver issues in western countries, affecting about 30% of American people in 2017 [2]. Prevalence of NAFLD is about 80% in overweight obese and about 20% in normal people [3]. Risk factors include diabetes, overweight, a high fructose diet and aging. [4]. Genetic risk factors of NAFLD are also known. High prevalence of NAFLD in presence of family history of diabetes type 2 [5]. High diet in omega-6 fatty acids and fructose sugar, has signify role in aggravation of disease from NAFLD to Non-alcoholic steatosis and fibrosis [6]. NAFLD can include either a steatosis alone; a steatosis with lobular or portal inflammation; or a steatosis with ballooning [7]. Common presentations are high transaminases and steatosis on ultrasonography. Sonography is useful in exclusion gallbladder stones (cholelithiasis) [3]. Investigations which are beneficial in diagnosis include ESR, blood sugar, serum albumin, renal function and coagulation profile [8]. Transient elastography (TE; Fibroscan) is a modest device with accepted accuracy to evaluate NAFLD [9]. TE has been admissible in many categories of liver disorders [10]. Treatment is generally with weight reduction by life style modification [11]. There is some evidence for Thiazolidenediones and vitamin E [1]. Treatment with pentoxifylline can has favorable effect in many small trials [12]. Synbiotics, have demonstrated improvements on inflammation in NAFLD patients [13]. For the AASLD, bariatric surgery can be presumed on an individual basis [8].

2. Patients and Methods:

This was a cross sectional study in Beni-Suef governorate performed in Beni-Suef university hospital, Beni-Suef Fever hospital, Health insurance hospital, and all the central hospitals in Beni-Suef governorate within six months from June 2020 till January 2021 involving 1000 non-diabetic ESRD patients on hemodialysis. Approval for our study protocol was taken by the Ethical Committee of Beni-Suef Faculty of Medicine verbal consents were obtained.

2.1 Inclusion criteria:

Adult patients on regular hemodialysis**.**

2.2 Exclusion criteria:

Diabetes mellitus Hepatitis C, hepatitis B

Chronic liver diseases ،Long duration of intake of hepatotoxic medication, Long history of alcohol intake.

I- History:

Age, Gender, Duration of hemodialysis,

Hypertension (duration –controlled or not)

Drug intake: Phosphate binders and Proton pump inhibitors, Vitamin D, Calcimimetic.

II-Full clinical examination:

With careful attention to:

Height, weight, and BMI. Blood Pressure, Cardiac examination. Abdominal examination: especially the liver.

III-Investigations:

Fasting glucose, post prandial glucose

Liver function tests Lipid profile. Fibroscan was done for evaluating fatty liver and /or liver fibrosis using FibroScan 502 Touch devices.

Statistical analysis of the data

Data obtained from the present study are presented as number and percent, mean and standard deviation (SD) or median and interquartile range (IQR). Categorical variables were compared using chi-square test while numerical variables were compared using one-way ANOVA or Kruskal-Wallis test as appropriate. All statistical tests were computed using SPSS 25 (IBM, USA) with p value less than 0.05 considered statistically significant.

3. Results:

The current study was conducted at Beni-Suef university hospital, Beni-Suef Fever hospital, Health insurance hospital, and all the central hospitals in Beni-Suef governorate within six months from June 2020 till January 2021 including 1000 adult ESRD patients on regular hemodialysis (545 males, and 455 female).

Table (1): Demographic & clinical data of studied cases (n = 1000)

Demographic and clinical data	No.	%
Gender		
Male	545	54.5
Female	455	45.5
Age (years)		
Min. – Max.	18.0 – 79.0	
Mean ± SD.	48.54 ± 15.05	
Median (IQR)	49.0 (35.50 – 61.0)	
HD duration (months)		
Min. – Max.	1.0 – 132.0	
Mean ± SD.	56.91 ± 38.07	
Median (IQR)	48.0 (24.0 – 89.50)	
BMI		
Min. – Max.	25.10 – 31.0	
Mean ± SD.	28.12 ± 1.52	
Median (IQR)	28.20 (27.0 – 29.20)	
HTN		
No	412	41.2
Yes	588	58.8

Systolic blood pressure (mmHg)	
Min. – Max.	110.0 – 170.0
Mean ± SD.	139.9 ± 20.54
Median (IQR)	140.0 (120.0 – 160.0)
Diastolic blood pressure (mmHg)	
Min. – Max.	60.0 – 100.0
Mean ± SD.	82.50 ± 12.95
Median (IQR)	80.0 (70.0 – 90.0)
Mean arterial blood pressure (mmHg)	
Min. – Max.	76.70 – 123.3
Mean ± SD.	101.6 ± 14.28
Median (IQR)	103.3 (90.0 – 113.30)

IQR: Inter Quartile Range

Table (1) shows that as for gender there were 545(54.5%) male and 455(45.5%) female with mean age (years) 48.54 (± 15.05SD) and range (18.0 – 79.0), with mean HD duration (months) 56.91 (± 38.07SD) and range (1.0 – 132.0**),** with mean BMI 28.12 **(**± 1.52SD) and range (25.10 – 31.0). AS regards HTN there were 588(58.8%) had HTN with mean Systolic blood pressure (mmHg) 139.9 (± 20.54SD) and range (110.0 – 170.0), mean Diastolic blood pressure (mmHg) 82.50 (± 12.95SD) and range (60.0 – 100.0), mean of Mean arterial blood pressure (mmHg) 101.6 (± 14.28SD) and range (76.70 – 123.3).

Table (2): CAP in studied cases (n = 1000)

CAP(dB/M)	No.	%
S0	503	50.3
S1	233	23.3
S1-S2	100	10.0
S2	67	6.7
S2-S3	10	1.0
S3	87	8.7
None NASH	503	50.3
NASH	497	49.7
S0	503	50.3
S1	233	23.3
S2:S3	264	26.4

Min. – Max.	100.0 – 398.0
Mean ± SD.	229.7 ± 76.35
Median (IQR)	216.0 (170.0 – 283.0)

Table (2) shows that as regard distribution of the studied cases according to CAP (dB/M) there were 503(50.3%) S0,233(23.3%) S1, 100(10.0%) S1-S2, 67(6.7%) S2,10(1.0%) S2-S3 and 87(8.7%) S3. There were 503(50.3%) None NASH and 497(49.8%) NASH with mean 229.7 (± 76.35SD) and range (100.0 – 398.0).

Table (3): Liver stiffness grades in studied cases (n=1000)

Liver stiffness grades (kPa)	**No.**	**%**
F0	508	50.8
F1	280	28.0
F2	57	5.7
F3	95	9.5
F4	60	6.0
F0	508	50.8
F1:F4	492	49.2
Min. – Max.	2.0 – 19.90	
Mean ± SD.	6.14 ± 3.90	
Median (IQR)	5.0 (3.50 – 6.85)	

Table (3) shows that as regard distribution of the studied cases according to liver stiffness grades there were 508(50.8%) F0, 280(28.0%) F1, 57(5.7%) F2,95(9.5%) F3 and 60(6.0%) F4. There were 508(50.8%) F0 and 492(49.2%) F1:F4 with mean 6.14 (± 3.90SD) and range (2.0 – 19.90).

Table (4): Comparison between none NASH and NASH patients as regards demographic and clinical data (n= 1000)

Demographic and clinical data	CAP(dB/M)				Test of Sig.	P
	None NASH (n = 503)		NASH (n = 497)			
	No.	%	No.	%		
Gender						
Male	288	57.3	257	51.7	χ^2= 1.200	0.273
Female	215	42.7	240	48.3		
Age (years)						
Min. – Max.	18.0 – 79.0		19.0 – 75.0		t= 2.462*	0.014*
Mean ± SD.	46.71 ± 15.33		50.39 ± 14.56			
Median	46.0		51.0			
HD duration (months)						
Min. – Max.	1.0 – 132.0		1.0 – 132.0		U= 18333.50	0.149
Mean ± SD.	54.25 ± 38.36		59.60 ± 37.68			
Median	48.0		57.0			
BMI						
Min. – Max.	25.10 – 31.0		25.10 – 31.0		t= 1.823	0.069
Mean ± SD.	27.98 ± 1.49		28.26 ± 1.54			
Median	28.0		28.40			
HTN						
No	197	39.2	215	43.2	χ^2= 0.632	0.427
Yes	305	60.8	283	56.8		
Systolic blood pressure (mmHg)						
Min. – Max.	110.0 – 170.0		110.0 – 170.0		t= 0.804	0.422
Mean ± SD.	140.70 ± 20.43		139.05 ± 20.66			
Median	140.0		140.0			
Diastolic blood pressure (mmHg)						
Min. – Max.	60.0 – 100.0		60.0 – 100.0		t= 0.251	0.802
Mean ± SD.	82.34 ± 13.34		82.66 ± 12.57			
Median	80.0		80.0			
Mean arterial blood pressure (mmHg)						
Min. – Max.	76.70 – 123.3		76.70 – 123.3		t= 0.235	0.814
Mean ± SD.	101.8 ± 14.48		101.5 ± 14.11			
Median	103.30		103.30			

χ^2: Chi square test t: Student t-test U: Mann Whitney test

IQR: Inter Quartile Range

Table (4) shows that there is statistically significant difference between NASH and different parameters as regards Age (years). This table shows that there is no statistically significant difference between NASH and different parameters as regards Gender, HD duration (months), BMI, HTN, Systolic blood pressure (mmHg), Diastolic blood pressure (mmHg) and Mean Arterial B.P (mmHg).

Table (5): Comparison between none NASH and NASH patients as regards liver stiffness grades and CAP value (n= 1000)

	CAP(dB/M)				**Test of Sig.**	**p**
	None NASH (n = 503)		**NASH (n = 497)**			
	No.	**%**	**No.**	**%**		
Liver stiffness grades						
F0	305	60.8	203	40.85		
F1	80	15.9	200	40.24		
F2	33	6.4	24	4.83	χ^2= 34.524*	<0.001*
F3	63	12.5	32	6.44		
F4	22	4.4	38	7.64		
F0	305	60.8	203	40.85	χ^2= 15.992*	<0.001*
F1:F4	197	39.2	295	59.15		
Min. – Max.	2.0 – 19.80		2.0 – 19.90		U= 17249.50*	0.017*
Mean ± SD.	5.91 ± 3.82		6.37 ± 3.97			
Median	4.60		5.30			
Cap value						
Min. – Max.	100.0 – 217.0		218.0 – 398.0		U= 0.000*	<0.001*
Mean ± SD.	167.32 ± 31.40		292.74 ± 52.99			
Median	170.0		283.0			

Fig (1): Liver stiffness grades in studied groups.

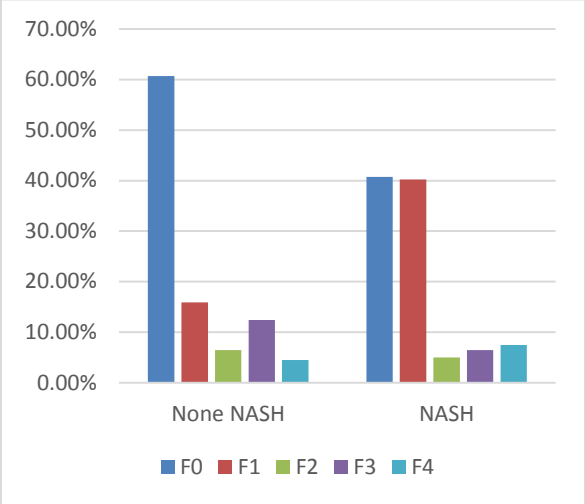

Fig (2) Mean Cap value in studied groups .

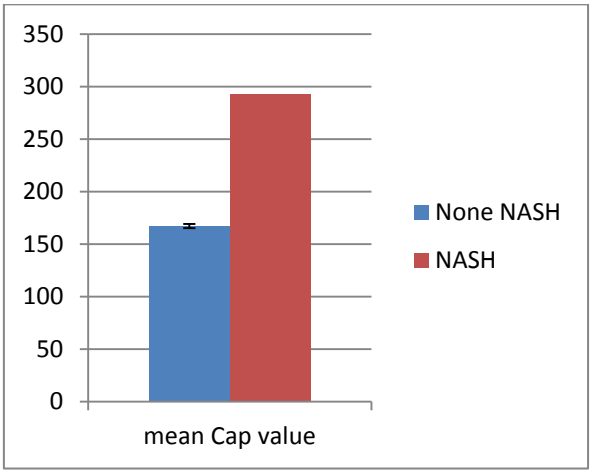

Table (5) and **figures (1, and 2)** show that there is high statistically significant difference between None NASH and NASH patients as regards liver stiffness grades and CAP value**.**

Table (6): Comparison between none NASH and NASH patients as regards laboratories (n= 1000).

Laboratories	CAP(dB/M)		Test of Sig.	P
	None NASH (n = 503)	NASH (n = 497)		
Serum triglyceride (mg/dL)				
Min. – Max.	130.0 – 196.0	140.0 – 294.0		
Mean ± SD.	161.1 ± 18.15	192.4 ± 33.54	t= 11.600*	<0.001*
Median	157.0	191.0		

Serum cholesterol (mg/dL)				
Min. – Max.	160.0 – 209.0	168.0 – 265.0	t= 13.740*	<0.001*
Mean ± SD.	182.6 ± 12.84	212.2 ± 27.65		
Median	181.0	210.0		
LDL (mg/dL)				
Min. – Max.	80.0 – 150.0	80.0 – 181.0	t= 5.277*	<0.001*
Mean ± SD.	114.5 ± 16.80	125.8 ± 25.07		
Median	113.0	125.0		
HDL (mg/dL)				
Min. – Max.	30.0 – 65.0	30.0 – 66.0	t= 0.791	0.429
Mean ± SD.	48.80 ± 9.25	48.03 ± 10.20		
Median	50.0	48.0		
AST (IU /L)				
Min. – Max.	11.0 – 115.0	15.0 – 115.0	U= 6715.50*	<0.001*
Mean ± SD.	31.67 ± 18.20	55.36 ± 21.56		
Median	29.0	50.0		
ALT(IU /L)				
Min. – Max.	9.0 – 108.0	13.0 – 102.0	U= 7125.0*	<0.001*
Mean ± SD.	33.27 ± 17.41	56.18 ± 21.44		
Median	32.0	52.0		

Table (6) shows that there is high statistically significant difference between None NASH and NASH patients as regards Serum triglyceride (mg/dL). Serum cholesterol (mg/dL), LDL (mg/dL), AST (IU /L) and ALT (IU /L). There is no statistically significant difference between NASH and different parameters as regards HDL (mg/dL).

Table (7): Correlation between CAP value, liver stiffness value and other factors in studied patients (n= 1000)

	CAP(dB/M)		**Liver stiffness (Kpa)**	
	r	**p**	**r**	**P**
Age (years)	0.087	0.081	0.012	0.810
HD duration (months)	0.108*	0.032*	-0.048	0.335
BMI	0.074	0.139	-0.011	0.833
Systolic blood pressure (mmHg)	-0.040	0.428	-0.033	0.507

Diastolic blood pressure (mmHg)	-0.004	0.931	-0.085	0.088
Mean arterial blood pressure (mmHg)	-0.022	0.665	-0.068	0.177
Serum triglyceride (mg/dL)	0.702*	<0.001*	0.182*	<0.001*
Serum cholesterol (mg/dL)	0.805*	<0.001*	0.063	0.206
LDL (mg/dL)	0.550*	<0.001*	0.004	0.940
HDL (mg/dL)	-0.103*	0.039*	0.037	0.455
AST (IU /L)	0.438*	<0.001*	-0.084	0.092
ALT(IU /L)	0.425*	<0.001*	-0.074	0.141

=r: Pearson coefficient

Table (7) shows that there is Correlation between CAP value and HD duration (months), HDL (mg/dL). There is strong Correlation between CAP(dB/M) value and Serum triglyceride (mg/dl), Serum cholesterol (mg/dL), LDL (mg/dL), AST (IU /L) and ALT (IU /L). This table shows that there is strong Correlation between liver stiffness (Kpa) value and Serum triglyceride (mg/dL).

Table (8): Comparison between CAP steatosis grades as regards demographic and clinical data (n= 1000)

Demographic and clinical data	**CAP steatosis grades**						**Test of Sig.**	**P value**
	S0 (n =503)		**S1 (n = 233)**		**S2:S3 (n =264)**			
	No.	**%**	**No.**	**%**	**No.**	**%**		
Gender								
Male	288	57.3	117	50.4	140	52.8	χ^2= 1.305	0.521
Female	215	42.7	115	49.6	126	47.2		
Age (years)								
Min. – Max.	18.0 – 79.0		19.0 – 75.0		20.0 – 74.0			
Mean ± SD.	46.71 ± 15.33		49.26 ± 14.39		51.38 ± 14.71		F= 3.527*	0.030*
Median	46.0		51.0		52.0			
HD duration (months)								
Min. – Max.	1.0 – 132.0		3.0 – 130.0		1.0 – 132.0			
Mean ± SD.	54.25 ± 38.36		67.19 ± 34.60		52.93 ± 39.15		H= 10.773*	0.005*
Median	48.0		66.0		44.50			

BMI								
Min. – Max.	25.10 – 31.0		25.10 – 31.0		25.20 – 31.0		F= 1.908	0.150
Mean ± SD.	27.98 ± 1.49		28.18 ± 1.61		28.33 ± 1.47			
Median	28.0		28.40		28.35			
HTN								
No	79	39.3	40	43.0	46	43.4	χ^2= 0.635	0.728
Yes	122	60.7	53	57.0	60	56.6		
Systolic blood pressure (mmHg)								
Min. – Max.	110.0 170.0		110.0 – 170.0		110.0- 170.0		F= 0.511	0.601
Mean ± SD.	140.7 ± 20.43		140.0 ± 20.54		138.2 ± 20.83			
Median	140.0		140.0		140.0			
Diastolic blood pressure (mmHg)								
Min. – Max.	60.0 – 100.0		60.0 – 100.0		60.0 – 100.0		F= 0.040	0.960
Mean ± SD.	82.34 ± 13.34		82.80 ± 12.63		82.55 ± 12.58			
Median	80.0		80.0		80.0			
Mean arterial blood pressure (mmHg)								
Min. – Max.	76.70- 123.3		76.70 – 123.3		76.70 – 123.3		F= 0.099	0.906
Mean ± SD.	101.8±14.48		101.9 ±14.27		101.1 ±14.02			
Median	103.3		103.3		101.7			

χ^2: Chi square test

F: F for ANOVA test H: H for Kruskal Wallis test
p: p value for association between CAP steatosis grades and different parameters
*: Statistically significant at $p \leq 0.05$
IQR: Inter Quartile Range

Fig (3): comparison between CAP steatosis grades according to mean Age (years).

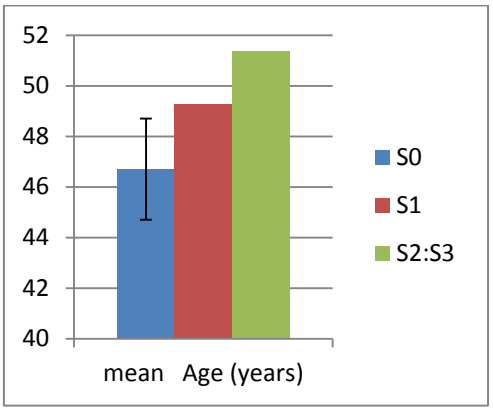

Fig (4): comparison between CAP steatosis grades according to mean HD duration (months).

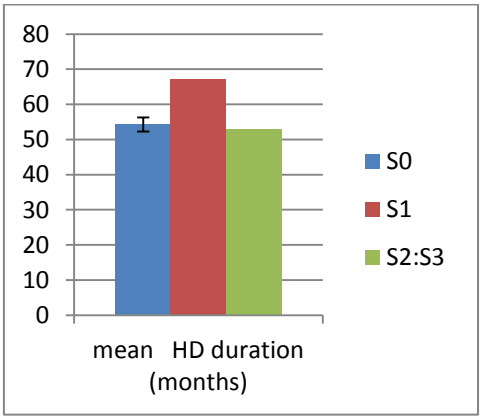

Table (8) and **figures (3 and 4)** show that there is statistically significant difference between CAP steatosis grades as regards Age (years) and HD duration (months). There is no statistically significant difference between CAP steatosis grades as regards Gender, BMI, HTN, Systolic blood pressure (mmHg), Diastolic blood pressure (mmHg), Mean arterial blood pressure (mmHg).

Table (9): Comparison between CAP steatosis grades as regards Liver stiffness grades and Cap value (n= 1000)

	CAP steatosis grades						**Test of Sig.**	**P**
	S0 (n =503)		**S1 (n = 233)**		**S2:S3 (n =264)**			
	No.	**%**	**No.**	**%**	**No.**	**%**		
Liver stiffness grades								
F0	305	60.6	113	48.5	90	34.0	χ^2= 40.967*	<0.001*
F1	80	15.9	88	37.8	113	43		
F2	33	6.4	12	5.1	12	4.5		
F3	64	12.7	10	4.3	22	8.3		
F4	22	4.4	10	4.3	27	10.2		
F0	305	60.6	113	48.5	90	34.	χ^2= 20.116*	<0.001*
F1:F4	198	39.4	120	51.5	174	66.0		
Min. – Max.	2.0 – 19.80		2.0 – 19.90		2.0 – 19.90		H= 10.171*	0.006*
Mean ± SD.	5.91 ± 3.82		5.69 ± 3.39		6.97 ± 4.34			
Median	4.60		5.0		5.70			
Cap value								
Min. – Max.	100.0 – 217.0		218.0 – 398.0		219.0 – 397.0		H= 300.024*	<0.001*
Mean ± SD.	167.32 ± 31.40		289.04 ± 59.0		295.98 ± 47.13			
Median	170.0		271.0		289.0			

p: p value for association between CAP steatosis grades and different parameters
*: Statistically significant at $p \leq 0.05$
IQR: Inter Quartile Range

(5): Comparison between CAP steatosis grades as regards Liver stiffness grades and Cap value.

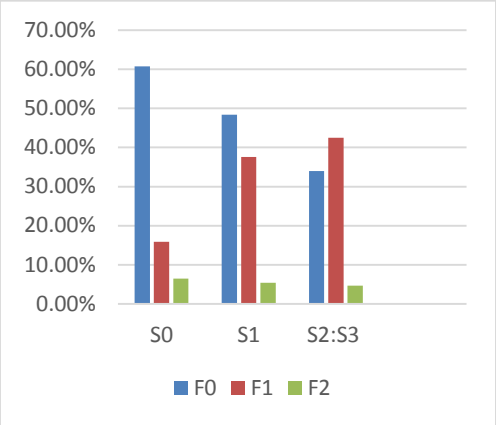

Table (9) and **figure (5)** show that there is high statistically significant difference between between CAP steatosis grades as regards Liver stiffness grades and Cap value.

Table (10): Comparison between CAP steatosis grades as regards laboratories (n= 1000)

Laboratories	CAP steatosis grades			Test of Sig.	p
	S0 (n =503)	S1 (n = 233)	S2:S3 (n =264)		
Serum triglyceride (mg/dL)					
Min. – Max.	130.0 – 196.0	140.0 – 247.0	140.0 – 294.0	F= 93.032*	<0.001*
Mean ± SD.	161.1 ± 18.15	180.4 ± 30.36	203.0 ± 32.75		
Median	157.0	172.0	202.0		
Serum cholesterol (mg/dL)					
Min. – Max.	160.0 – 209.0	168.0 – 258.0	170.0 – 265.0	F= 108.827*	<0.001*
Mean ± SD.	182.6 ± 12.84	205.2 ± 28.58	218.3 ± 25.40		
Median	181.0	198.0	219.5		
LDL (mg/dL)					
Min. – Max.	80.0 – 150.0	80.0 – 174.0	80.0 – 181.0	F= 14.488*	<0.001*
Mean ± SD.	114.5 ±	124.2 ±	127.3 ±		

	16.80	25.47	24.75		
Median	113.0	118.0	129.0		
HDL (mg/dL)					
Min. – Max.	30.0 – 65.0	30.0 – 66.0	30.0 – 66.0		
Mean ± SD.	48.80 ± 9.25	48.73 ± 10.37	47.42 ± 10.05	F= 0.766	0.466
Median	50.0	49.0	46.50		
AST (IU /L)					
Min. – Max.	11.0 – 115.0	15.0 – 100.0	15.0 – 115.0		
Mean ± SD.	31.67 ± 18.20	54.91 ± 21.67	55.75 ± 21.56	H= 132.115*	<0.001*
Median	29.0	51.0	50.0		
ALT(IU /L)					
Min. – Max.	9.0 – 108.0	13.0 – 99.0	14.0 – 102.0		
Mean ± SD.	33.27 ± 17.41	55.54 ± 21.67	56.74 ± 21.32	H= 124.187*	<0.001*
Median	32.0	51.0	52.0		

F: F for ANOVA test H: H for Kruskal Wallis test

Table (10) shows that there is high statistically significant difference between between CAP steatosis grades as regards Serum triglyceride (mg/dL), Serum cholesterol (mg/dL), LDL (mg/dL), AST (IU /L) and ALT (IU /L).

Table (11): Comparison between liver stiffness grades as regards cap and liver stiffness value (n= 1000)

	Liver stiffness grades				**Test of Sig.**	**P**
	F0(n =508)		**F1:F4 (n = 492)**			
	No.	**%**	**No.**	**%**		
CAP(dB/M)						
S0	305	60.1	198	40.1		
S1	113	22.2	120	24.4		
S1-S2	25	4.9	75	15.2	χ^2= 26.706*	<0.001*
S2	35	6.9	32	6.6		
S2-S3	0	0.0	10	2.0		
S3	30	5.9	57	11.7		
None NASH	305	60.1	198	40.1	χ^2= 15.992*	<0.001*
NASH	203	39.9	294	59.9		
S0	305	60.1	198	40.1	χ^2= 20.116*	<0.001*
S1	113	22.2	120	24.4		
S2:S3	90	17.7	174	35.5		
Min. – Max.	100.0 – 396.0		100.0 – 398.0		U= 15162.0*	<0.001*
Mean ± SD.	214.55 ± 73.65		245.35 ± 76.12			
Median	202.0		244.0			
Liver stiffness value						
Min. – Max.	2.0 – 5.0		5.0 – 19.90		U= 20.0*	<0.001*
Mean ± SD.	3.54 ± 0.89		8.81 ± 3.99			
Median	3.60		6.90			

χ^2: Chi square test U: Mann Whitney test

p: p value for association between Liver stiffness grades and different parameters

Fig (6): Comparison between liver stiffness grades as regards cap and liver stiffness value**.**

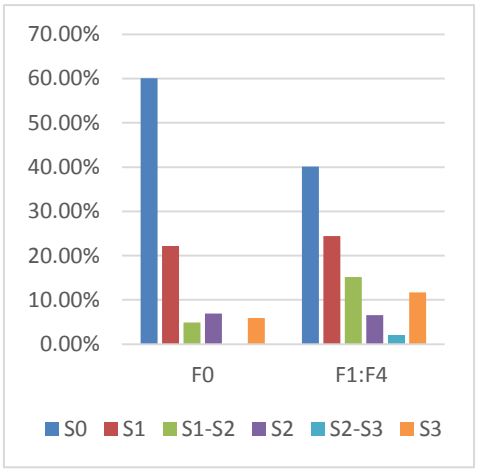

Table (11) and **figure (6)** show that there is high statistically significant difference between liver stiffness grades as regards CAP(dB/M) and liver stiffness value.

Table (12) Comparison between liver stiffness grades as regards laboratories (n= 1000)

Laboratories	Liver stiffness grades		Test of Sig.	P
	F0(n =508)	F1:F4 (n = 492)		
Serum triglyceride (mg/dL)				
Min. – Max.	130.0 – 244.0	131.0 – 294.0	t= 5.190*	<0.001*
Mean ± SD.	168.93 ± 25.65	184.65 ± 34.18		
Median	164.0	178.0		
Serum cholesterol (mg/dL)				
Min. – Max.	160.0 – 258.0	160.0 – 265.0	t= 3.706*	<0.001*
Mean ± SD.	192.63 ± 23.77	202.18 ± 27.58		
Median	187.0	198.0		
LDL (mg/dL)				
Min. – Max.	80.0 – 173.0	80.0 – 181.0	t= 1.324	0.186
Mean ± SD.	118.71 ± 20.75	121.63 ± 23.24		
Median	116.0	120.0		

HDL (mg/dL)				
Min. – Max.	30.0 – 66.0	30.0 – 66.0		
Mean ± SD.	47.95 ± 9.30	48.90 ± 10.16	t= 0.974	0.331
Median	49.0	49.0		
AST (IU /L)				
Min. – Max.	11.0 – 115.0	11.0 – 115.0		
Mean ± SD.	42.52 ± 23.64	44.41 ± 22.72	U= 18723.0	0.271
Median	37.0	40.0		
ALT(IU /L)				
Min. – Max.	9.0 – 108.0	10.0 – 102.0		
Mean ± SD.	43.64 ± 23.22	45.73 ± 21.98	U= 18575.50	0.219
Median	38.0	41.0		

p: p value for association between Liver stiffness grades and different parameters
*: Statistically significant at $p \leq 0.05$
IQR: Inter Quartile Range

Fig (7): Comparison between liver stiffness grades as regards mean Serum triglyceride (mg/dL).

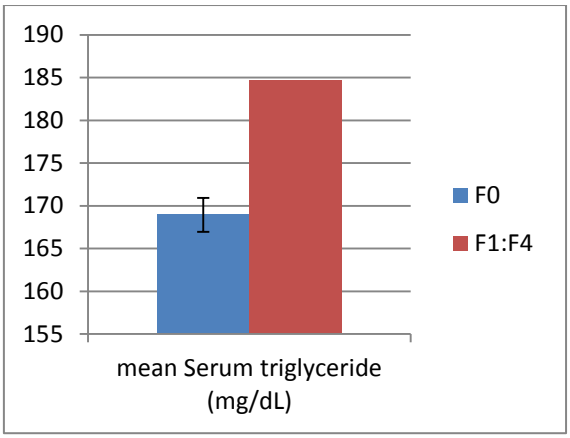

Fig (8): Comparison between liver stiffness grades as regards mean Serum cholesterol (mg/dL)**.**

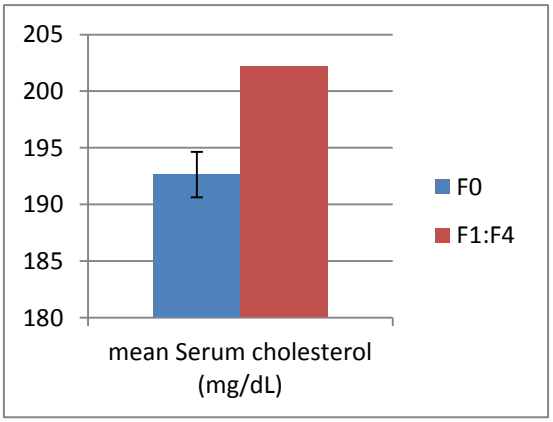

Table (12) and **figure (7 and 8)** show that there is a high statistically significant difference liver stiffness grade as regards Serum triglyceride (mg/dL) and Serum cholesterol (mg/dL)

Table (13): Correlation between CAP value, liver stiffness value and other different parameters in none NASH patients (n= 1000)

	CAP(dB/M)		Liver stiffness (Kpa)	
	r	**p**	**R**	**P**
Age (years)	-0.056	0.426	0.028	0.697
HD duration (months)	0.096	0.177	-0.014	0.841
BMI	-0.028	0.689	0.078	0.269
Systolic blood pressure	-0.025	0.727	-0.042	0.555
Diastolic blood pressure	<0.001	1.000	-0.076	0.284
Mean arterial blood pressure	-0.012	0.871	-0.066	0.349
Serum triglyceride	0.504*	<0.001*	0.145*	0.040*
Serum cholesterol	0.658*	<0.001*	-0.015	0.832
LDL	0.526*	<0.001*	-0.026	0.710
HDL	-0.193*	0.006*	0.113	0.111
AST	0.146*	0.039*	-0.177*	0.012*
ALT	0.128	0.070	-0.159*	0.024*

Table (13) shows that there is correlation between CAP (dB/M) value and HDL (AST (IU /L). There is strong correlation between CAP (dB/M) value and Serum triglyceride (mg/dL), Serum cholesterol (mg/dL), LDL (mg/dL). This table shows that there is correlation between liver stiffness value and Serum triglyceride (mg/dL), AST (IU /L), ALT (IU /L).

Table (14): Correlation between CAP value, liver stiffness value and other different parameters in NASH patients (n= 1000)

	CAP(dB/M)		**Liver stiffness (Kpa)**	
	r	**p**	**R**	**P**
Age (years)	-0.005	0.948	-0.018	0.796
HD duration (months)	0.088	0.219	-0.091	0.202
BMI	0.014	0.841	-0.105	0.140
Systolic blood pressure	-0.005	0.949	-0.020	0.774
Diastolic blood pressure	-0.044	0.539	-0.097	0.173
Mean arterial blood pressure	-0.028	0.692	-0.068	0.342
Serum triglyceride	0.614*	<0.001*	0.204*	0.004*
Serum cholesterol	0.743*	<0.001*	0.062	0.381
LDL	0.656*	<0.001*	-0.003	0.970
HDL	-0.091	0.201	-0.024	0.733
AST	-0.020	0.776	-0.098	0.167
ALT	-0.038	0.593	-0.091	0.203

Table (14) shows that there is strong correlation between CAP value and Serum triglyceride (mg/dL), Serum cholesterol (mg/dL) and LDL (mg/dL). There is correlation between liver stiffness value and Serum triglyceride (mg/dL).

4. Discussion:

Hemodialysis (HD) patients have high mortality rate in compare to general people have nearby ages. This bad prognosis is due to cardiovascular mortality and repeated infections. Beside the other risk factors such as hypertension, type 2 diabetes and hyperlipidemia. Preceding studies showed that NAFLD is an important risk factor correlated with cardiovascular incident in hemodialysis patients [14]. Many non-invasive methods that are estimated as a procedure of diagnosis of hepatic fibrosis or steatosis, but still the optimum method for conclusive diagnosis is a liver biopsy. Because it is an invasive procedure with many probable grave multipliers, it may be not a favorable method. Recently, a study showed that controlled attenuation parameter (CAP), estimated with transient elastography (TE) (Fibroscan ®), could detect accurately fibrosis grades [15]. In this study we target to detect the incidence of non-alcholic steatohepatitis between non-diabetic hemodialysis patients in Beni-Suef governorate. In this study we found that there were 545(54.5%) male and 455(45.5%) female with mean age(years) 48.54 (± 15.05SD) and range (18.0 – 79.0), with mean HD duration (months) 56.91 (± 38.07SD) and range (1.0 – 132.0), with mean BMI 28.12 (± 1.52SD) and range (25.10 – 31.0), there were 588(58.8%) had HTN with mean Systolic blood pressure (mmHg) 139.9 (± 20.54SD) and range (110.0 – 170.0), mean Diastolic blood pressure (mmHg) 82.50 (± 12.95SD) and range (60.0 – 100.0), mean of Mean arterial blood pressure (mmHg) 101.6 (± 14.28SD) and range (76.70 – 123.3). Behairy et al. 2019[16] found that there were 50 ESRD patients on HD [30 Males, 20 females], with mean age 48.62 ± 13.13 yrs., HD mean duration was 4.02 ± 2.57 yrs., mean of BMI 28.13 ± 1.02 (Kg/m2), Prevalence of hypertension was (56%). Wu et al. 2018 [17] found that the mean age was 56.0 ± 11.7 years, and the mean hemodialysis duration was 87.8 ± 63.5 months. By ultrasonography 19 (26.7%) patients had NAFLD and 52(73.2%) patients did not. Our results showed that as regards laboratories there were mean FBS 84.97 (± 10.01SD) and range (69.0 – 105.0), mean PPBS 109.2 (± 9.68SD) and range (91.0 – 125.0), mean Serum triglyceride (mg/dL) 176.67 (± 31.13SD) and range (130.0 – 294.0), mean Serum cholesterol (mg/dL) 197.3 (± 26.12SD)

and range (160.0 – 265.0), mean LDL (mg/dL) 120.2 (± 22.03SD) and range (80.0 – 181.0), mean HDL (mg/dL) 48.42 (± 9.73SD) and range (30.0 – 66.0), mean AST (IU /L) 43.45 (± 23.18SD) and range (11.0 – 115.0), mean ALT(IU /L) 44.67 (± 22.61SD) and range (9.0 – 108.0). Wu et al. 2018[17] found that serum ALT 16 ± 9 (U/L), AST 20 ± 9 (U/L), Bilirubin 0.33 ± 0.13 (mg/dl), Cholesterol 185 ± 33 (mg/dL), Triglycerides 156 ± 86 (mg/dL), LDL 105 ± 27 (mg/dL), HDL 45 ± 9 (mg/dL), alkaline phosphatase 104 ± 45 (mg/dL). In this study we cleared that according to CAP (dB/M) there were 503(50.3%) S0, 233(23.3%) S1, 100(10.0%) S1-S2, 67(6.7%) S2, 10(1.0%) S2-S3 and 87(8.7%) S3. Behairy et al. 2019[16] found that CAP steatosis grades among HD patients with NAFLD were 14(28.0%) patients with S1, 7(14.0%) S1 – S2, 2(4.0%) S2, and 6(12.0%) with S3 grade. Mikolasevic et al. 2014[18] found that the degrees of liver steatosis were estimated by CAP values: 10(18.9%) patients had grade 1, 14 (26.4%) grade 2 and 29(54.7%) grade 3. In this study we demonstrated that according to liver stiffness grades there were 508(50.8%) F0, 280(28.0%) F1, 57(5.7%) F2, 95(9.5%) F3 and 60(6.0%) F4. There were 508(50.8%) F0 and 492(49.3%) F1:F4 with mean 6.14 (± 3.90SD) and range (2.0 – 19.90). Behairy et al. 2019[16] found that Mean ± SD of Liver stiffness value was 6.80 ± 6.08 (Kpa) in NAFLD patients, as 14(48.3%) patient with F1 grade, 3(10.2%) patients grade from F2-F3 and 12(41.4 %) F0 patients. In study in our hands we found that there is statistically significant difference between NASH and different parameters as regards Age (years). Choe et al. 2020[19] found that patients in the NAFLD group had a significantly higher body mass index (BMI; 27.2 ± 16.3 vs. 24.1 ± 3.6 kg/m2) and there is insignificant difference between groups as age and sex and blood pressure. Mikolasevic et al. 2014[18] found that there were no statistically significant differences due to BMI and FAT between the two groups. In this thesis we found that there is high statistically significant difference between None NASH and NASH patients as regards liver stiffness grades and CAP value. Behairy et al. 2019[16] found that there was a positive correlation between NAFLD and liver stiffness grade (X2 = 12.808, MCP = 0.002) and CAP value. In this study we cleared that there is high statistically significant difference between None NASH and NASH patients as regards Serum triglyceride, Serum cholesterol, LDL, AST and ALT. Behairy et al. 2019 [16] found that there is significant statistical correlation between existence of NAFLD and increasing level of liver enzymes, serum Cholesterol, Triglycerides and LDL ($P<0.01$). Choe et al. 2020[19] found that patients in the NAFLD group had a significantly higher triglyceride (192 vs. 119 mg/dL), and total cholesterol (178.7 ± 42.4 vs.

163.2 ± 44.9 mg/dL) than those in the non-NAFLD group (all $P < 0.05$). Although the prevalence of dyslipidemia was significantly higher in the NAFLD group ($P < 0.001$), patient in NAFLD group had a significantly higher ALT, AST than non-NAFLD group ($P<0.001$ for both). Mikolasevic et al. 2014[18] found that there was highly significant difference between HD patients with NAFLD and HD patients without NAFLD as regards ALT and AST, there is significant difference between two groups as regards Cholesterol level and triglyceride. In this study we demonstrated that there is Correlation between CAP value and HD duration (months), HDL (mg/dL). There is strong Correlation between CAP(dB/M) value and Serum triglyceride, serum cholesterol, LDL, AST and ALT, there is strong Correlation between liver stiffness (Kpa) value and Serum triglyceride (mg/dL). Teeratorn et al. 2020[20] found that the predictors of significant stiffness in NAFLD were male gender (odd ratio [OR] 2.87, 95% CI 1.09–7.56, $p < 0.033$) and hyperlipidemia (OR 2.75, 95% CI 1.05–7.21, $p = 0.039$. Mikolasevic et al. 2014[18] found that there was positive correlation between grade of steatosis and serum creatinine concentration, the systolic B.P and the CRP level; but with negative correlation with eGFR and levels of serum iron. Our results showed that there is high statistically significant difference between between CAP steatosis grades as regards Liver stiffness grades and Cap value. Bellan, M et al. 2019[21] found that there is highly significant difference between Cap steatosis grades and Liver stiffness. In this study we found that there is high statistically significant difference between CAP steatosis grades as regards Serum triglyceride, Serum cholesterol, LDL, AST and ALT. Chan et al. 2014[22] found that there was highly significant difference between CAP steatosis grades as regards BMI, Serum triglyceride, Serum cholesterol, LDL, AST and ALT. In study in our hands we demonstrated there is high statistically significant difference liver stiffness grades as regards Serum triglyceride (mg/dL) and Serum cholesterol (mg/dL). Chan et al. 2014[22] found that there were high statistically significant difference liver stiffness grades as regards age, BMI, FBS, TG, HDL, LDL, ALP, ALT, AST, and CAP.

5. Conclusion and Recommendations:

In this study we concluded that there is a high incidence of Non-alcoholic fatty liver disease among non-diabetic patients on regular Hemodialysis in Beni-Suef governorate, significantly correlated with increasing degree of liver stiffness. Further studies on larger sample size and on large geographical scale to emphasize our conclusion.

6. References:

1. Nonalcoholic Fatty Liver Disease & NASH. National Institute of Diabetes and

Digestive and Kidney Diseases. November 2016. Retrieved 7 November 2018.

2. Rich NE, Oji S, Mufti AR, Browning JD, Parikh ND, Odewole M, Mayo H, and Singal AG (2018). "Racial and Ethnic Disparities in. Nonalcoholic Fatty Liver Disease Prevalence, Severity, and Outcomes in the United States: A Systematic Review and Meta-analysis". Clinical Gastroenterology and Hepatology. 16 (2): 198–210.e2. doi: 10.1016/j.cgh.2017.09.041. PMC 5794571. PMID 28970148.
3. Younossi Z, Anstee QM, Marietti M, Hardy T, Henry L, Eslam M, George J, and Bugianesi E (2018). "Global burden of NAFLD and NASH: trends, predictions, risk factors and prevention". Nature Reviews. Gastroenterology & Hepatology. 15 (1): 11–20. doi:10.1038/nrgastro.2017.109. PMID 28930295.
4. Mann, J., Valenti, L., Scorletti, E., Byrne, C., & Nobili, V. (2018). Nonalcoholic fatty liver disease in children. In Seminars in liver disease (Vol. 38, No. 01, pp. 1-13).
5. Friedman SL, Neuschwander-Tetri BA, Rinella M, and Sanyal AJ (2018). "Mechanisms of NAFLD development and therapeutic strategies". Nature Medicine. 24 (7): 908–922. doi:10.1038/s41591-018-0104-9. PMC 6553468. PMID 29967350.
6. Vancells Lujan, P., Viñas Esmel, E., & Sacanella Meseguer, E. (2021). Overview of Non-Alcoholic Fatty Liver Disease (NAFLD) and the Role of Sugary Food Consumption and Other Dietary Components in Its Development. Nutrients, 13(5), 1442.
7. European Association for the Study of the Liver (EASL); European Association for the study of Diabetes (EASD); European Association for the study of Obesity (EASO) (2016). "EASL-EASD-EASO Clinical Practice Guidelines for the management of non-alcoholic fatty liver disease". Journal of Hepatology. 64 (6): 1388–402. doi: 10.1016/j.jhep.2015.11.004. PMC 5644799. PMID 27062661.
8. Pagana, K. D., & Pagana, T. J. (2017). Mosby's Manual of Diagnostic and Laboratory Tests-E-Book. Elsevier Health Sciences.
9. Xie, L. T., Yan, C. H., Zhao, Q. Y., He, M. N., & Jiang, T. A. (2018). Quantitative and noninvasive assessment of chronic liver diseases using two-dimensional shear wave elastography. World journal of gastroenterology, 24(9), 957.
10. Moreno, C., Mueller, S., & Szabo, G. (2019). Non-invasive diagnosis and biomarkers in alcohol-related liver disease. Journal of hepatology, 70(2), 273-283.
11. Chalasani N, Younossi Z, Lavine JE, Charlton M, Cusi K, Rinella M, Harrison

SA, Brunt EM, and Sanyal AJ (2018). "The diagnosis and management of nonalcoholic fatty liver disease: Practice guidance from the American Association for the Study of Liver Diseases". Hepatology. 67 (1): 328–357.

12. Raziel A, Sakran N, Szold A, and Goitein D (2015). "Current solutions for obesity-related liver disorders: non-alcoholic fatty liver disease and non-alcoholic steatohepatitis" (PDF). The Israel Medical Association Journal. 17 (4): 234–8. PMID 26040050.
13. Hadi A, Mohammadi H, Miraghajani M, and Ghaedi E (2018). "Efficacy of synbiotic supplementation in patients with nonalcoholic fatty liver disease: A systematic review and meta-analysis of clinical trials: Synbiotic supplementation and NAFLD". Critical Reviews in Food Science and Nutrition: 1–12. doi:10.1080/10408398.2018.1458021. PMID 29584449.
14. Cozzolino, M., Mangano, M., Stucchi, A., Ciceri, P., Conte, F., & Galassi, A. (2018). Cardiovascular disease in dialysis patients. Nephrology Dialysis Transplantation, 33(suppl_3), iii28-iii34.
15. Lonardo, A., Ballestri, S., Guaraldi, G., Nascimbeni, F., Romagnoli, D., Zona, S., & Targher, G. (2016). Fatty liver is associated with an increased risk of diabetes and cardiovascular disease.Evidence from three different disease models: NAFLD, HCV and HIV. World journal of gastroenterology, 22(44), 9674.
16. Behairy, M., Elshaarawy, A., Aly, H., & Wasfy, M. (2019). Sp645 survey of non-alcoholic fatty liver disease among non-diabetic haemodialysis patients by transient elastography. Nephrology Dialysis Transplantation, 34(Supplement_1), gfz103-SP645.
17. Wu, P. J., Chen, J. B., Lee, W. C., Ng, H. Y., Lien, S. C., Tsai, P. Y., ... & Chiou, T. T. Y. (2018). Oxidative stress and nonalcoholic fatty liver disease in hemodialysis patients. Biomed Research International, 2018.
18. Mikolasevic, Ivana; Orlic, Lidija; Milic, Sandra; Zaputovic, Luka; Lukenda, Vesna; Racki, Sanjin (2014). Non-Alcoholic Fatty Liver Disease Proven by Transient Elastography in Hemodialysis Patients: Is It a New Risk Factor for Adverse Cardiovascular Events. Blood Purification, 37(4), 259–265. doi:10.1159/000360270.
19. Choe, A. R., Ryu, D. R., Kim, H. Y., Lee, H. A., Lim, J., Kim, J. S., ... & Yoo, K. (2020). Noninvasive indices for predicting nonalcoholic fatty liver disease in patients with chronic kidney disease. BMC nephrology, 21(1), 1-11.
20. Teeratorn, N., Piyachaturawat, P., Thanapirom, K., Chaiteerakij, R., Sonsiri, K., Komolmit, P., ... & Treeprasertsuk, S.

(2020). Screening for non-alcoholic fatty liver disease in community setting: A cohort study using controlled attenuation parameter-transient elastography. JGH Open, 4(2), 245-250.

21. Bellan, M., Rigamonti, C., Giacomini, G. M., Makmur, G., Marconi, C., Nicosia, F., ... & Pirisi, M. (2019). Liver Stiffness, Not Fat Liver Content, Predicts the Length of QTc Interval in Patients with Chronic Liver Disease. Gastroenterology research and practice, 2019.
22. Chan, W. K., Nik Mustapha, N. R., & Mahadeva, S. (2014). Controlled attenuation parameter for the detection and quantification of hepatic steatosis in nonalcoholic fatty liver disease. Journal of gastroenterology and hepatology, 29(7), 1470-1476.