Serum Myostatin in Liver Cirrhosis: a Marker beyond Malnutrition

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Background and study aim: Compensated and decompensated cirrhotic patients are both affected by variable degrees of malnutrition. Myostatin is secreted by muscle cells and adipocytes. It causes inhibition of skeletal muscle growth. The present work aimed to demonstrate the relationship between serum myostatin and the degree of malnutrition and to show its role in prognosis in comparison to the model for end-stage liver diseases (MELD) score.
Patients and Methods: We included seventy patients with liver cirrhosis and twenty healthy controls in this study. Assessment of malnutrition was done by subjective global assessment (SGA) in addition to measurements of body mass index (BMI), mid-arm muscle circumference (MAMC), and serum myostatin.

Results: Among 70 patients with liver cirrhosis serum myostatin levels were significantly higher in malnourished cirrhotic patients (U=41.5, P=0.001). It was considerably higher in Child C than in Child B or Child A patients (P < 0.05). Roc curve analysis revealed that serum myostatin in liver cirrhotic patients at a cut-off> 6.1 can differentiate malnourished from well-nourished patients with a sensitivity of 98.04% and, a specificity of 84.2%. MELD score and serum myostatin were positively correlated (P < 0.05).
Conclusion: High serum myostatin is associated with profound degrees of malnutrition. It is valuable in liver disease prognosis as it is positively correlated with the MELD score.

INTRODUCTION

In chronic liver disease, sarcopenia defined as: loss of muscle mass and/or muscle power, is a common finding that is related to complications and mortality in cirrhotic patients [1]. Patients with malnutrition undergoing liver transplantation are more susceptible to infections, and longer ICU stay with a higher mortality [2.[

The etiology of malnutrition in patients with liver cirrhosis is multifactorial including decreased dietary intake due to anorexia, nausea, and vomiting. Additionally, intolerance to food with a high-fat content as there is decreased bile salt production in cirrhosis. Additionally, small intestinal mucous membrane edema because of hypoalbuminemia leads to decreased nutrient absorption. All these factors result in a reduction in glucose stores that leads to depletion of muscle mass and a dependency on protein stores for energy [3.[

Sarcopenia occurs as a result of an imbalance between protein synthesis and protein breakdown in the skeletal muscles. In liver cirrhosis protein imbalance occurs due to several mechanisms including chronic inflammation, hyperammonemia, and endocrine abnormalities among others [4].

Sarcopenia is identified through assessment of muscle mass, power, and performance [5]. Anthropometric measurements are used for assessing the patient's nutritional status as triceps skin fold thickness, body mass index (BMI), mid-arm muscle circumference (MAMC), and Subjective global assessment score (SGA.(

The subjective global assessment (SGA) is a nutrition assessment tool that refers to an overall evaluation of a patient's history and physical examination and uses structured clinical parameters to diagnose malnutrition [5]. Underweight cirrhotic patients (BMI < 14 kg/m2) have a higher risk of mortality and should be admitted to the hospital for the initiation of intensive nutritional support [6.[

Myostatin, a myokine, plays a crucial role in muscle mass homeostasis. Myostatin is mainly produced by the skeletal muscles and is a strong negative regulator of muscle mass [7]. High levels of serum myostatin induce muscle wasting [8]. There is growing evidence on the impact of muscle wasting on the prognosis of liver disease, therefore myostatin has been a common research subject of different recent studies [9,10 .[

Based on the Child-Pugh scoring, the rate of sarcopenia increases as the severity of liver disease increases [11]. Also, liver cirrhosis is associated with increased serum myostatin levels, furthermore, high myostatin levels have been correlated with increased mortality rates among cirrhotic patients [12]. In patients undergoing evaluation for liver transplantation, a high serum myostatin was observed in comparison with controls [13] with a higher mortality over a 7-year follow-up [14 .[

Child-Pugh and model for end-stage liver disease (MELD) scores are non-invasive methods that are used in predicting the prognosis of liver cirrhosis, other indicators are still needed. Ideal serum biomarkers are needed to predict the prognosis of cirrhosis. Many efforts have been made to explore the prognostic value of various serum biomarkers at different stages of liver cirrhosis. Serum myostatin is a promising biomarker, that has a high value in patients with liver cirrhosis than in controls [15 .[

This study aimed to demonstrate the relationship between Myostatin and the degree of malnutrition and to show its role in prognosis in comparison to the model for end-stage liver diseases (MELD) score .

METHODOLOGY

The study was an observational, cross-sectional study carried out on 90 individuals attending the Tropical Medicine Department, at Alexandria Main University Hospital.

Group I: 70 patients with liver cirrhosis that were assessed by the subjective global assessment (SGA) and subdivided according to the presence or absence of malnutrition according to SGA .

Group II: 20 healthy controls.

Ethical approval was obtained, and informed consent was taken from each patient included in the study.

Exclusion criteria :
1. Female sex.
2. Heart failure.
3. Renal impairment.
4. Chronic obstructive pulmonary disease (COPD).
5. Diabetes mellitus.
6. Obesity (BMI more than 30).
7. Alcoholic hepatitis, Non-alcoholic steatohepatitis (by normal liver enzymes and ultrasound assessment).
8. Hepatocellular carcinoma (by normal alpha-fetoprotein and ultrasound assessment.(

Malnutrition was assessed by:
1. Subjective global assessment (SGA): groups were divided into well-nourished and malnourished according to the SGA score. SGA was obtained by filling subjective global assessment form.[16[
2. Anthropometric measurements such as; muscle mass, Body mass index (BMI), and biochemical variables, were taken afterward for each group (well-nourished and malnourished .(
3. Muscle mass measurements: Dry mass index:([weight – TBW]/height2) [17], triceps Fold (TFT) [18], and mid-arm-muscle- circumference (MAMC).[19] (TBW: total body water: 2.447 – (0.09145 x age) + (0.1074 x height in centimeters) + (0.3362 x weight in kilograms) = total body water (TBW) in liters.(
4. Muscle depletion was diagnosed according to standard values for the general population matched for age and sex as previously reported: <5th percentile .
5. Controlling nutritional status (CONUT) score: it was calculated using serum

albumin, total cholesterol concentrations, and total lymphocytic count. [20[

MELD and Child-Pugh scoring systems were calculated .

Assessment of serum myostatin was done by ELISA; Kit (E-EL-H1437) [21[

RESULTS

Routine Laboratory investigations and demographic data

As regards to subject's age, in the control group, it ranged between 25-31 years with a mean of 27.80 ± 2.15 years while in the cirrhosis group, it ranged between 42-78 years with a mean of 56.87 ±7.50 years. Statistically significant differences were found between the two groups .

A significant difference was found between cirrhotic patients and controls regarding serum platelets. (p = 0.005(

Serum alanine aminotransferase (ALT), total bilirubin, albumin, and international normalized ratio (INR), all were significantly different between cirrhotic patients and controls. (p value= 0.005, <0.001, <0.001 and, <0.001 respectively(

No significant difference was found between cirrhosis and controls regarding renal functions.

Table 1: Routine Laboratory investigations and demographic data

	Cirrhosis (n = 70)	Control (n = 10)	test of significance	P
Age Mean ± SD. Median	56.87 ± 7.50 56	27.80 ± 2.15 28	25.847*	<0.001*
Hemoglobin (g/dl) Mean ± SD. Median	12.06 ± 1.70 12.05	12.54 ± 0.66 11.5	t= 1.65	0.107
WBCs (10^9/l) Mean ± SD. Median	5.23 ± 2.09 4.75	4.79 ± 2.34 4.27	U= 321.5	0.678
Platelets (10^9/l) Mean ± SD. Median	260 ± 91.11 109.5	197.30 ± 51.78 183	U= 157.50*	0.005*
ALT (U/L) Mean ± SD. Median	33.04 ± 21.62 25	19.60 ± 6.83 18.5	U=156.50*	0.005*
AST (U/L) Mean ± SD. Median	39.41 ± 26.16 28	29.30 ± 6.17 29	U=334.5	0.821
Total Bilirubin (mg/dl) Mean ± SD. Median	1.88 ± 1.51 1.3	0.65 ± 0.31 0.55	U= 89.00*	<0.001*
Albumin (g/dl) Mean ± SD. Median	3.06 ± 0.86 3.05	4.14 ± 0.49 4.05	t= 5.781*	<0.001*
INR Mean ± SD. Median	1.36 ± 0.36 1.3	0.98 ± 0.18 1	t=5.362*	<0.001*
Creatinine (mg/dl) Mean ± SD. Median	1.08 ± 0.39 1	0.97 ± 0.27 0.95	U=303	0.492
BUN (mg/dl) Mean ± SD. Median	22.40 ± 13.05 19	17.9 – 3.70 18.5	U=269.5	0.239

U: Mann Whitney   t: Student t-test   p: p-value for comparing between the
two groups WBC: white blood cells   LT: alanine aminotransferase   AST: aspartate aminotransferase
INR: international normalized ratio   BUN: blood urea nitrogen

Nutritional assessment

The subjective global assessment (SGA)

In this study 39.2 % had a high degree of malnutrition according to SGA, 33.3% had moderate malnutrition and 27.5 % had a mild degree of malnutrition.
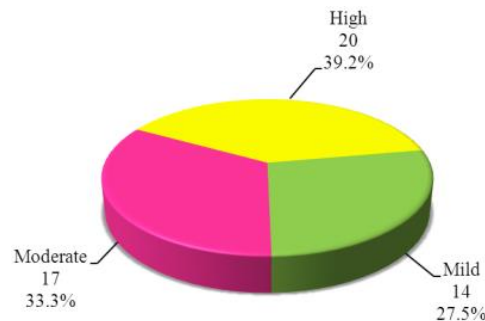

Figure (1): Distribution of the studied cases according to the degree of malnutrition (SGA) in Malnourished (m = 51) (SGA: subjective global assessment)

Body mass index
Dry BMI

In a Mild degree of malnutrition, dry BMI ranged between 11.0 – 26.0 kg/m ^{2} with a mean of. 21.43 ± 4.80 kg/m ^{2}, while in the Moderate group, it ranged between 10.0 – 27.0 kg/m ^{2} with a mean of 22.88 ± 5.18 kg/m ^{2} The third group representing the high SGA ranged between 10.0 – 27.0 kg/m ^{2} with a mean of 20.95 ± 5.62 kg/m

^{2}. Dry BMI was of no statistically significant differences between the three groups, P=0.443.

Mid-arm circumference

Mid-arm circumference ranged from 21.5- 38 cm with a median of 27 cm in the well-nourished group and from 17-33 cm with a median of 23 cm in the malnourished group and that was statistically significant. (p= 0.017)
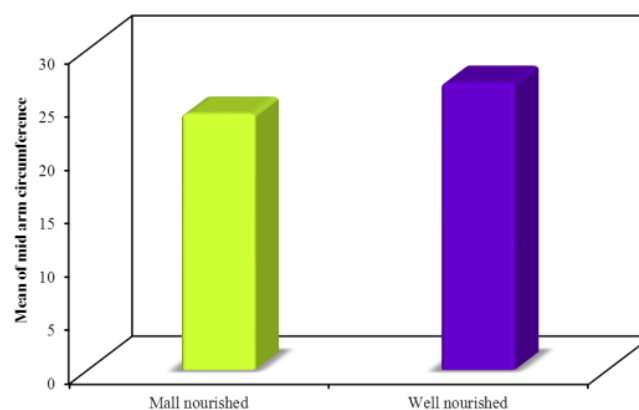

Figure (2): Comparison between the two studied groups according to mid-arm circumference (cm)

Triceps fold measurements and controlling nutritional status (CONUT) score

For triceps fold measurements there was a significant reduction in a malnourished group rather than well-nourished patients (p=0.001)

regarding the controlling nutritional status (CONUT) score, a significant increase in its values in malnourished patients was noticed. (p= 0.001).

Table (2):   Comparison between the two studied groups according to triceps fold (cm) and CONUT score

	Malnourished (n = 51)	Well-nourished (n = 19)	U	P
Triceps fold				
Min. – Max.	0.30 – 8.0	2.0 – 11.0		
Mean ± SD.	3.04 ± 2.19	5.63 ± 2.71	213.00*	<0.001*
Median	2.0	5.0		
CONUT				
Min. – Max.	2.0 – 13.0	1.0		
Mean ± SD.	7.29 ± 3.34	1.0 ± 0.0	0.00	<0.001*
Median	8.0	1.0		

U: Mann Whitney test   CONUT score: controlling nutritional status score
p: p-value for comparing between the two groups.

MELD and Child-Pugh scoring systems correlation to malnutrition

Malnutrition was observed in patients with Child grades B and C with a mean of 8.04 ± 2.23 (p = 0.002),

also, malnutrition was associated significantly with a higher MELD score with a mean of 13.43 ± 5.25 (p= 0.001)

Table (3): Comparison between the two studied groups according to different parameters

	Malnourished (n = 51)		Well-nourished (n = 19)		Test of sig.	P
MELD score						
Min. – Max.	5.0 – 26.0		6.0 – 11.0		U= 116.00*	<0.001*
Mean ± SD.	13.43 ± 5.25		7.05 ± 1.54			
Median	14.0		6.0			
Child score	No.	%	No.	%		
A	16	31.4	16	84.2		
B	16	31.4	1	5.3	χ^2= 15.636*	<0.001*
C	19	37.3	2	10.5		
Min. – Max.	5.0 – 12.0		5.0 – 13.0		U= 256.00*	0.002*
Mean ± SD.	8.04 ± 2.23		6.32 ± 2.24			
Median	8.0		6.0			

χ^2: Chi-square   U: Mann Whitney test   MELD score: a model for end-stage liver disease

SGA correlation to MELD and Child-Pugh scoring systems

A positive significant correlation was found between the degree of malnutrition (SGA) with

both MELD score (p < 0.001) and child score (p=0.019).

Table (4): Relation between degree of malnutrition (SGA) with MELD and Child score

	Degree of malnutrition (SGA)			Test of Sig.	P
	Mild (n = 14)	Moderate (n = 17)	High (n = 20)		
MELD score Min. – Max. Mean ± SD. Median	5.0 – 14.0 8.71 ± 2.79 8.50	7.0 – 26.0 13.24 ± 5.57 11.0	10.0 – 25.0 16.90 ± 3.46 17.0	F= 16.067*	<0.001*
Sig. bet. Groups	p_1=0.011*, p_2<0.001*, p_3=0.027*				
Child score Min. – Max. Mean ± SD. Median	5.0 – 11.0 7.0 ± 2.0 6.0	5.0 – 11.0 7.59 ± 1.91 7.0	5.0 – 12.0 9.15 ± 2.23 10.0	H= 7.958*	0.019*
Sig. bet. Groups	p_1=0.461, p_2=0.008*, p_3=0.045*				

SGA: subjective global assessment　　　　　　　　　MELD score: model for end-stage liver disease

F: F for ANOVA test, pairwise comparison between each 2 groups was done using a Post Hoc Test (Tukey)

H: H for Kruskal Wallis test, pairwise comparison bet. each 2 groups were done using Post Hoc Test (Dunn's for multiple comparisons test)

p: p-value for comparing between the three groups　　　　p_1: p-value for comparing between Mild and Moderate

p_2: p-value for comparing between Mild and High　　　　p_3: p-value for comparing between Moderate and High

*: Statistically significant at $p \leq 0.05$

SGA correlation to hepatic encephalopathy

A positive significant correlation was found between the degree of malnutrition and the presence of hepatic encephalopathy. (p=0.001)

Table (5): Relation between degree of malnutrition (SGA) with hepatic encephalopathy

	Degree of malnutrition (SGA)						χ^2	P
	Mild (n = 14)		Moderate (n = 17)		High (n = 20)			
	No.	%	No.	%	No.	%		
Hepatic Encephalopathy Absent	11[a]	78.6	12[a]	70.6	4[b]	20.0	14.528*	0.001*
Present	3[a]	21.4	5[a]	29.4	16[b]	80.0		

χ^2: Chi-square test　　　MC: Monte Carlo　　　SGA: a subjective global assessment

p: p-value for comparing between the two groups.

Serum myostatin

Higher Serum myostatin was found in the malnourished group (median: 10.7 ng/ml) rather than in the well-nourished group (median:4.2 ng/ml) which is of significant difference (p=<0.001)

Table (6): comparison of serum Myostatin between malnourished and well-nourished

	Malnourished (n = 51)	Well-nourished (n = 19)	U	P
Serum myostatin ng/ml				
Min. – Max.	2.0 – 16.0	1.20 – 8.0		
Mean ± SD.	10.94 ± 3.17	4.41 ± 1.98	41.5*	<0.001*
Median	10.70	4.20		

U: Mann Whitney test p: p value for comparing between the two groups.

Also, serum myostatin correlated positively with the degree of malnutrition (p= <0.001), where higher levels were seen in severe degrees of malnutrition (median: 14.15 ng/ml) rather than in moderate degree of malnutrition (median: 10.3 ng/ml) and mild degree of malnutrition (median: 7.4 ng/ml)

Table (7): Relation between degrees of malnutrition (SGA) with Serum myostatin

	Degree of malnutrition (SGA)			H	P
	Mild (n = 14)	Moderate (n = 17)	High (n = 20)		
Serum myostatin (ng/ml)					
Min. – Max.	2.0 – 8.0	9.10 – 11.70	9.0 – 16.0		
Mean ± SD.	7.01 ± 1.47	10.43 ± 0.86	14.13 ± 1.42	41.425*	<0.001*
Median	7.40	10.30	14.15		
Sig. bet. Groups	p_1=0.002*, p_2<0.001*, p_3=0.001*				

H: H for Kruskal Wallis test, pairwise comparison between each 2 groups were done using Post Hoc Test (Dunn's for multiple comparisons test)

p: p-value for comparing between the three groups p_1: p-value for comparing between Mild and Moderate

p_2: p-value for comparing between Mild and High p_3: p-value for comparing between Moderate and High

*: Statistically significant at p ≤ 0.05

When discriminating malnourished and well-nourished cases, the ROC curve for serum myostatin was significant (<0.001) and showed that the cutoff point discriminating control from cases was 17ng/ml, with sensitivity of 98%, specificity of 84%, positive predictive value of 94.3 % and negative predictive value of 94.1%. Test accuracy was 94.3%.

Table (8): Agreement (sensitivity, specificity) for serum myostatin to diagnose mall nourished from well-nourished

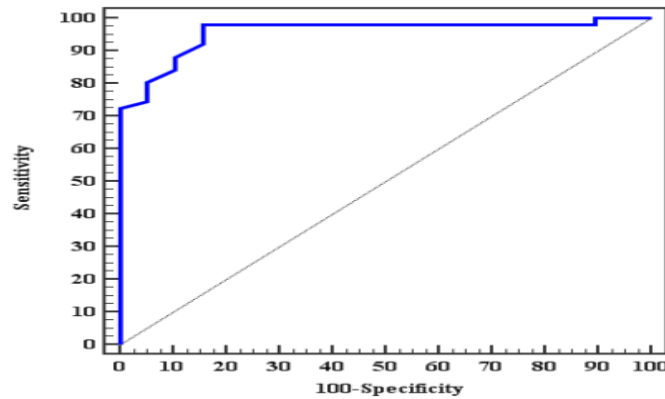|	AUC	P	95% C.I		Cut off	Sensitivity	Specificity	PPV	NPV	Test Accuracy
			LL	UL						
Serum myostatin	0.957	<0.001*	0.910	1.00	>6.1	98.04	84.21	94.3	94.1	94.3

Figure (3): ROC curve for serum myostatin to diagnose malnourished from well-nourished

When comparing serum levels of myostatin in cirrhotic patients and control, we found significantly higher levels of serum myostatin in cirrhotic patients rather than in controls(p=<0.001)

Table (9): comparison of serum myostatin between cirrhotic and control

	Cirrhosis (n = 70)	Control (n = 10)	U	P
Serum myostatin (ng/ml)				
Min. – Max.	1.20 – 16.0	2.30 – 5.60	97.0*	<0.001*
Mean ± SD.	9.17 ± 4.11	4.13 ± 1.19		
Median	9.20	4.20		

U: Mann Whitney test p: p value for comparing between the two groups.

When comparing the serum level of myostatin to the presence or absence of hepatic encephalopathy, we found significantly higher levels in patients with hepatic encephalopathy (p=<0.001)

Table (10):   Relation between hepatic encephalopathy with Serum myostatin

	Hepatic encephalopathy		U	P
	Absent (n = 43)	Present (n = 8)		
Serum myostatin (ng/ml)				
Min. – Max.	1.20 – 14.70	2.0 – 16.0	234.0*	<0.001*
Mean ± SD.	7.56 ± 3.41	11.73 ± 3.86		
Median	7.50	13.70		

U: Mann Whitney test p: p value for comparing between the two groups.

A higher significant correlation was noticed between serum myostatin level and child scoring (p=<0.001). Also, serum myostatin level, bilirubin level, and INR level were all significantly positively correlated, but serum myostatin was negatively correlated with serum albumin level.

Table (11):   Relation between Child score with serum myostatin

	Child score			H	P
	A (n = 32)	B (n = 17)	C (n= 21)		
Serum myostatin (ng/ml)				21.673*	<0.001*
Min. – Max.	1.20 – 14.0	6.90 – 14.70	2.0 – 16.0		
Mean ± SD.	6.73 ± 3.37	10.81 ± 2.76	11.55 ± 4.10		
Median	7.20	10.60	13.50		
Sig. bet. Groups	p_1=0.001*, p_2<0.001*, p_3=0.546				

H: H for Kruskal Wallis test, pairwise comparison between each 2 groups was done using Post Hoc Test (Dunn's for multiple comparisons test)

p: p-value for comparing between the three groups p_1: p-value for comparing between A and B

p_2: p-value for comparing between A and C p_3: p-value for comparing between B and C

Myostatin and MELD Score

After the exclusion of HCC from our study, myostatin was correlated to MELD within the three categories where p=0.015 in Mild SGA p=0.035 in Moderate SGA, and p=0.005 in high SGA. A statistically significant difference and a positive correlation were found between myostatin and MELD in the three subgroups of malnutrition.
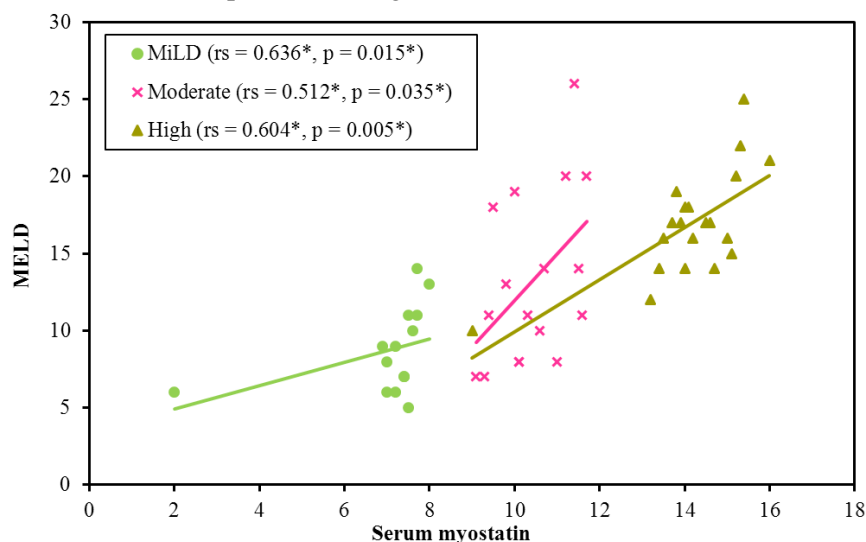

Figure (4):   Correlation between Serum myostatin with MELD score

MELD: model for end-stage liver disease
p: p-value for comparing between the two groups.
Rs: Pearson correlation coefficient

When discriminating High MELD with prioritization of liver transplantation from the low MELD category, the ROC curve for serum myostatin was significant (<0.001) and showed that the cutoff point discriminating priority to liver transplantation was 7.5 ng/ml, with a sensitivity of 85.1%, specificity of 93.9%, positive predictive value of 95.2%, and negative predictive value of 81.6%.

Table (12): Cutoff point of serum myostatin level that prioritizes liver transplantation

Agreement (sensitivity, specificity) for serum myostatin to diagnose >7 MELD from ≤7

| | AUC | P | 95% C. I | | Cut off | Sensitivity | Specificity | PPV | NPV | Test Accuracy |
			LL	UL						
Serum myostatin ng/ml	0.936	<0.001*	0.883	0.988	>7.5	85.11	93.94	95.2	81.6	94.3

AUC: area under the curve value   PPV: positive predictive value   NPV: negative predictive
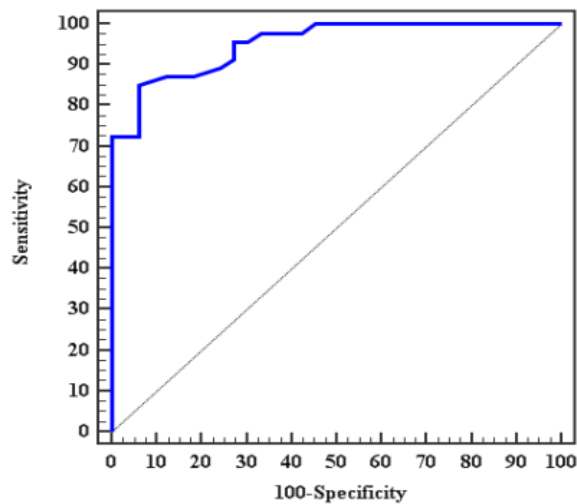

Figure (5): ROC curve for cutoff point of serum myostatin that prioritizes liver transplantation

DISCUSSION

Cirrhosis is the normal progression of liver disease, presenting with signs of decompensation as ascites, hepatic encephalopathy, and bleeding tendency mainly esophageal varices. Malnutrition and sarcopenia worsen the prognosis of cirrhotic patients. Malnutrition is a common complication of liver cirrhosis that occurs in 20-50% of patients, where 20% of compensated cirrhotic have malnutrition, on the other hand, 50% of decompensated cirrhotic have severe malnutrition [22].

Malnutrition affects the course of liver cirrhosis negatively; however, it remains a potentially reversible prognostic marker in cirrhosis [23]. Myostatin is mainly expressed in skeletal muscle, however other tissues also express myostatin. It is a major upstream regulator of skeletal muscle function and an inhibitor of skeletal muscle mass and growth [24].

The present work aimed to demonstrate the relationship between myostatin and the degree of malnutrition and to show its role in prognosis in comparison to the model for end-stage liver diseases (MELD) score.

In our study, cirrhotic patients were subdivided according to the Subjective global assessment (SGA) into three categories: Mild, Moderate, and severely malnourished 27%, 33.3%, and 39.2% respectively. This comes in agreement with Vierira et al [25] Their study cirrhotics were subdivided according to SGA into the same subgroups with small variations in the percentage showing mild, Moderate, and severe malnutrition with 61.5%, 41%, and 20.5% respectively.

As regards dry body mass index (BMI), there was no statistically significant difference between the three groups, where the moderately malnourished group had a higher mean than the mild and the severely malnourished groups which were almost equivalent. This was in accordance with Vierira et al. [25] who showed a significantly higher ideal dry BMI % in a

moderately malnourished group than the two other groups .

In our study, the mid-arm muscle circumference (MAMC) showed a statistically significant difference between the malnourished and the well-nourished groups where the malnourished MAMC was below the 5th percentile range and lower than the well-nourished group. This comes in agreement with Vierira et al. [25], who agreed with our results showing a statistically significant difference between the two groups, where the ideal MAMC % was lower in a malnourished group than the well-nourished one .

In our study, the triceps fold thickness (TFT) showed a statistically significant difference between the two groups, where the malnourished group showed a lower TFT than the well-nourished one. This was in accordance with Vierira et al. [25] where the ideal TFT % was lower in a malnourished group rather than the well-nourished group and a low TFT diagnosed malnutrition in 93.6% of patients.

Also, there was an agreement with our results in Pashayee Khamenei et al [26] since there was a statistically significant difference between well-nourished and malnourished groups, where TFT was lower in malnourished than in well-nourished.

They stated that TFT decreases with the severity of malnutrition. Both parameters of malnutrition, MAMC, and TFT were studied by Houissa et al. [27] who showed a significant difference between malnourished and well-nourished groups with a cut-off 60% reduction of normal value .

In our study, a statistically significant difference was found regarding the degree of malnutrition and the incidence of hepatic encephalopathy, where the incidence increases with the worsening of the nutrition status. This agrees with Merli et al. [28] who explained the relation between malnutrition and hepatic encephalopathy by muscular involvement in ammonia metabolism. Also, we studied the incidence of hepatic encephalopathy in relation to serum myostatin showing a higher level of serum myostatin in cases of frequent hepatic encephalopathy.

Serum albumin was lower significantly in patients than in control P<0.001. This also agrees with Vieria et al. [25] who stated a significant decrease in the ideal albumin % in malnourished

patients in comparison to well-nourished ones. INR was higher significantly in patients than in control P<0.001, bilirubin was also significantly higher in patients than in control P<0.001.

Myostatin was then correlated to synthetic liver function including albumin, prothrombin activity, and bilirubin showing a negative correlation, same as for Nishikawa et al. [29] where myostatin was also correlated to albumin and prothrombin activity showing negative correlation too, however, they added on more significant correlations such as correlating myostatin to psoas muscle index (PMI), and branched-chain amino acids (BCA)/Tyrosine ratio both showing a negative correlation .

In our study myostatin showed a sensitivity of 98.04%and specificity of 84.21% for malnutrition. Myostatin cut-off value was 6.5 microgram/dl.

Limitations in the study included the small sample size and the reduced number of patients with hepatic encephalopathy, a larger sample size is needed to verify further the relation between hepatic encephalopathy and serum myostatin.

CONCLUSION

Serum myostatin is a sensitive tool for nutritional deficiency in liver cirrhosis patients. Serum Myostatin represents a promising target to prioritize patients for liver transplantation post-TB care is essential to improving long-term outcomes.

Author Contributions:

Somasundram Pillay and Davashni Pillay conceptualized the study and oversaw the entire process, including methodology and manuscript preparation. Both authors contributed to the revision of the manuscript and approved the final 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 dataː

-drafting the paper or revising it criticallyː

-approving the submitted version.

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

Ethical consideration: The research was conducted following the Declaration of Helsinki and national and institutional standards.

HIGHLIGHTS

- Serum myostatin is a sensitive tool for nutritional deficiency in liver cirrhosis patients.

- Serum myostatin correlates positively with the MELD score and CHILD scoring system.

- Serum myostatin represents a promising target for predicting the clinical outcomes of patients with liver cirrhosis and prioritizing listing for liver transplantation.

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