Assessment of Malnutrition in Patients with Chronic Liver Disease

Sushant[1], Madhavi Sarkari[2]

[1, 2]Department of Medicine, B. R. D Medical College, Gorakhpur, UP, India

[2]Corresponding Author Email ID: *madhvisarkari[at]yahoo.co.in*

Abstract: *Introduction: Malnutrition is a common feature of chronic liver disease and increases the mortality and morbidity rate among cirrhosis patients. This study aimed to investigate the prevalence of malnutrition in patientswith chronic liver disease and its correlation with Child - Turcotte - Pugh (CTP) and Model for End - Stage Liver Disease (MELD) scores. Methodology: This points observational study included patients with chronic liver disease (CLD), graded by severity based on CTP and MELD scores. The clinic - demographic parameters, along with biochemical and radiological parameters, will be recorded. Sarcopenia was assessed according to EWGSOP2 criteria, and correlation of sarcopenia was done with CTP and MELD scores Results: A total of 105CLD patients were enrolled in the study. The majority of patients were male, 88.6%, while 11.4% were female. The prevalence of sarcopenia was 93.3% in males and 6.7% in females. The mean serum albumin, MELD and CHILD PUGH scores were higher in sarcopenic females, while other clinical parameters were lower in sarcopenic females. The mean MELD and CHILD PUGH scores were higher in sarcopenic males, while other clinical parameters were lower in sarcopenic males. Conclusion: Malnutrition is prevalent among CLD patients and chronic liver disease patients are typically more malnourished. Sarcopenia is a common complication of liver cirrhosis and adverse outcomes and poor survival rates.*

Keywords: Sarcopenia, Model for End - Stage Liver Disease, Child - Turcotte - Pugh, Chronic Liver Disease

1. Introduction

A progressive decline in liver function characterises chronic liver disease (CLD). Among the tasks of the liver are the generation of clotting factors and other proteins, the detoxification of toxic metabolic byproducts, and the excretion of bile. This ongoing process of inflammation, destruction, and regeneration of liver parenchyma leads to fibrosis and cirrhosis. [1] Cirrhosis is the last stage of chronic liver disease, characterised by disturbance of hepatic architecture, creation of extensive nodules, vascular reorganisation, neo - angiogenesis, and extracellular matrix deposition. Patients with CLD suffer from a significant impairment that can lead to protein - calorie malnutrition (PCM). Malnutrition affects the vast majority of CLD patients. About 20% of patients with compensated cirrhosis and up to 60% of those with severe disease are malnourished. [2, 3] In patients awaiting a liver transplant, it is, therefore, more prevalent than among cancer patients and nearly inevitable. EASL advocates incorporating sarcopenia assessment into nutritional screening for individuals with chronic liver disease, utilising functional and body composition imaging techniques. Sarcopenia evaluation is considered more accurate than anthropometric assessments because it directly assesses muscle structure and function and eliminates the confounding effects of sarcopenic obesity. According to the guidelines of the European Society for Clinical Nutrition and Metabolism (ESPEN), using simple bedside tools such as SGA, anthropometry, or handgrip strength to identify patients at risk of malnutrition is adequate. It should be used to screen further patients who may require nutrition therapy if nutritional needs are unmet. [4, 5] There is still no consensus regarding the optimal method for quantifying and classifying malnutrition. Consequently, this study aimed to assess the nutritional status of CLD patients.

2. Material and Methods

The Department of Medicine conducted this observational study from January 2022 to December 2023. This research enrolled all 18 - to - 65 - year - old patients with chronic liver disease, regardless of aetiology, who were outpatients and inpatients at the BRD medical college. In contrast, patients with Cirrhosis with HCC or other malignant tumours, Severe diseases of extrahepatic organs, such as COPD or heart failure, Active tuberculosis, thyrotoxicosis, neuromuscular disease, and Long - term immobile status, are not candidates for liver transplantation. Patients on long - term corticosteroid therapy, HIV infection as the infectiology team most closely monitor these patients, specific endocrinopathies such as Graves' disease and Cushing syndrome, and noncompliance with follow - up medical consultations and therapies are risk factors for relapse. Hepatic encephalopathy and encephalopathy of the liver patients who refused to provide consent were excluded. All participants in the study were subjected to a blood examination and various test of nutritional status assessments. The CTP and MELDNa scores determined the severity of each subject. The diagnosis of sarcopenia was made using EWGSOP2 criteria. Anthropometry – Mid - upper arm circumference measured using a steel measuring tape at the midpoint between the acromion process and the olecranon, per standard protocol. The cut - off value for males is 23.3 cm, and for females, it is 22.6 cm. The midthigh circumference will be measured at the midpoint between the inguinal crease and the proximal margin of the patella on the right thigh. The psoas muscle area (cm^2) was measured by a trained operator using the NIH ImageJ software, which enables specific tissue demarcation using previously reported Hounsfield unit thresholds (for psoas muscle, - 29 to +150). Normalised the psoas muscle area at the L3 vertebra to the patient's height squared (m^2). The sarcopenia cut - off for psoas muscle index is less than 5.7

mm^2/mm for men and 3.57 mm^2/mm for women. Area of the psoas muscle = the mean of the maximal cross - sectional area at LS. Psoas muscle index = right Psoas area plus left Psoas area divided by two. The isometric hand grip strength (HGS) was measured using a portable dynamometer. The device measures force in kilograms with an accuracy of 0.1kg. Each participant was required to perform the task twice with each hand. The highest result from each hand was used as a measure for these analyses. According to the Asian Working Group for Sarcopenia's consensus report, inadequate grip strength is defined as 26 kg for men and 18 kg for women.

Statistical Analysis:
Statistical analysis was performed using SPSS software (SPSS Inc., Chicago, IL, USA) for the Windows program (15.0 version). The continuous variables were evaluated by mean (standard deviation) or range value when required. The dichotomous variables were presented in number/frequency and wereanalyzed using Chi - square or Fisher Extract test. For comparison of the means, analysis by Student t - test and Mann - Whitney U test with a 95% confidence interval were used. Cut - off values were analysed using ROC analysis. A p - value of < 0.05 or 0.001 was regarded as significant.

3. Results

Of the enrolled 105 patients, most were males, 93 (88.60%) with a mean age of 41.69±9.93 years. [Table - 1; Figure - 1] The mean serum albumin was 2.70±0.32, the mid - arm circumference was 23.41±4.35cm, and the mid - thigh circumference was 37.39±6.46cm. The Psoas muscle area was recorded as 7.51±1.10cm², Psoas muscle area index was 4.74±0.67mm²/mm, hand grip strength 22.19±3.39 Kg, MELD Score 18.54±4.18 and Child - Pugh Score was 9.81±2.42. [Table - 2] The presence of reduced hand grip strength was higher among the male population 83 (93.3%) than among females 6 (6.7%). Also, in the case of the absence of reduced hand grip strength, it was higher in males than females. The hand grip according to gender was highly significant. [Table - 3] Most of our study's patient population was sarcopenic (85.7%). In the study, the association between gender and sarcopenia was highly significant. [Table - 4; Figure - 2] Further, we noted that in sarcopenic males, the mean serum albumin was 2.70±0.32cm, the mid - arm circumference was 23.57±3.92, the mid - thigh circumference was 37.11±6.56cm. MELD score was 19.17±3.51, and the child Pugh score was 10.13±2.19. All these parameters were significant among sarcopenic males. [Table - 5; Figure - 3] Similar was the case with females, where the serum albumin (p=0.0013*), mid - arm circumference (p<0.0001*), mid - thigh circumference (p<0.0001*), psoas muscle area (p<0.0001*), handgrip strength (p<0.0001*), MELD score (p<0.0001*), CTP (p<0.0001*) were associated with sarcopenia. [Figure - 4]Additionally, we observed a significant positive correlation between serum albumin, mid - arm circumference, mid - thigh circumference and PM area with PM index, while a negative correlation between MELD and Child - Pugh score was observed. There was a negative correlation between hand grip strength with the P. M index and age, although insignificant. MELD and Child - Pugh

scores were negatively correlated with HGS. [Figure - 5 and 6]

4. Discussion

In the present study, the mean age of patients was 41.69±9.93 years. There were 54.3% of patients in the age group 20 - 40 years, 42.9% of patients in 41 - 60 years and only 2.9% of patients above 60 years of age. Most patients were male, 93 (88.60%), while 12 (11.40%) were females in the total study population.85.7% of the study population was sarcopenic, while 14.3% had no sarcopenia. On the contrary, **Evuri P et al.** [6] observed that the majority of the patients in their study were not sarcopenic (45.6%), followed by those who had sarcopenia (24.6%). Patients were aged between 41 - 50 years, followed by 51 - 60 years. At the same time, they observed male preponderance, which was similar to the present study's finding.84 (93.3%) of males and 6 (6.7%) of females had sarcopenia. The presence of sarcopenia was higher in the age group of 20 - 40 years of males [47 (56.0%)], which was similar in the case of females also [3 (50.0%)]. For the age group above 60 years, only 2 (2.4%) males and 1 (16.7%) female had sarcopenia, while there was no population of non - sarcopenia in this age group. There was no significant association between the age of the population and sarcopenia, but a significant association was observed regarding gender. On the contrary, **Evuri P et al.** [6] observed a significant association between Sarcopenia and age distribution. The highest confirmed sarcopenia cases were seen in the age group >60 years (41.2%), but no such association was observed in gender. According to the study of **Montano - Loza et al.** [7], among 669 patients, 68% were males, and 45% had sarcopenia. Despite the findings of **Ebadi M et al.** [8] and **Kim G et al.** [9] that sarcopenia is more prevalent in males with chronic liver disease, **Evuri P et al.** [6] study showed no statistical difference between men and women for sarcopenia. Women have greater fat reserves than men and utilise fat reserves more frequently than muscular ones. [10] Therefore, women's fat reserves are drained more than men's skeletal muscle mass. Additionally, changes in sex hormones may influence the rate of skeletal muscle turnover. [11]In the present study, the mean serum albumin was higher in the sarcopenic population [2.70±0.32] and non - sarcopenic [2.68±0.40]. Mid - arm and thigh circumferences were significantly higher in patients with no sarcopenia than in those with sarcopenia. The mean P. M (pectoralis muscle) area was also significantly higher in the non - sarcopenic population [9.01±1.82] than in the sarcopenic population [7.43±0.92]. HGS was also higher in non - sarcopenic patients [25.53±4.94] compared to the sarcopenic patients [21.80±2.92]. In contrast, the MELD score and Child - Pugh score were higher in sarcopenic patients [19.26±3.65; 10.16±2.23, respectively] than in non - sarcopenic patients [14.27±4.68; 7.73±2.52, respectively]. Both malnutrition and sarcopenia are characterised by decreased muscle mass, although a loss of function more frequently accompanies sarcopenia. Additionally, as a result of calorie restriction, patients with malnutrition have a reduction in fat mass, although this is typically not the case with sarcopenia. Hence, functional tests of strength and performance are done to rule out malnutrition. [12] Further, **Evuri P et al.** [6] showed a higher level of albumin in non - sarcopenic

patients [3.31±0.78] than in sarcopenic patients [2.81±0.71]. They showed that MELD and Child - Pugh scores were higher in patients with sarcopenia, while hand grip was higher in patients without sarcopenia. Some studies found no correlation between sarcopenia and the death - predicting hepatic dysfunction scores (Child - Pugh and MELD). [7, 13, 14] Others observed a correlation and recommended that integrating sarcopenia assessment in Child - Pugh and MELD scores could make it easier to forecast a cirrhotic patient's death. [7, 13, 14] The sarcopenic group in this study had a higher mean CTP and MELD score, but there was no substantial correlation between the two. The prognosis of sarcopenic cirrhotic patients is much poorer than that of non - sarcopenic cirrhotic patients [9]. There was a statistically significant difference between sarcopenic and non - sarcopenic participants in our study. These findings are in complete accordance with the findings of **Evuri P et al.** [6]. Correspondingly, **Montano - Loza et al.** [7] found that sarcopenic patients had significantly higher serum levels of bilirubin, MELD andChild–Pugh scores than non - sarcopenic patients. As sarcopenia is independently related to a double mortality rate, the modification of MELD to incorporate sarcopenia (MELD - sarcopenia) improves mortality prediction in cirrhotic patients. The apparent advantage of changing MELD to include sarcopenia was greatest among individuals with low MELD scores, who are conventionally considered to have a low mortality risk. If sarcopenia is present, it is equivalent to adding 10 points to the MELD score, illustrating its significance. In another research, patients with cirrhosis and refractory ascites were treated with 20 g of human albumin twice per week over the long term. Patients treated with albumin showed a significantly lower incidence of 1 - year mortality than those treated with conventional treatment (41.6% vs 65.5%; P = 0.032) and also had a decreased incidence of HE, ascites, and SBP [15]. We also evaluated the clinical parameters concerning the gender of sarcopenic and non - sarcopenic females. In sarcopenic females, the mean of serum albumin was [2.65±0.25], MELD [20.50±5.58], and Child - Pugh scores [11.24±3.02] were significantly higher compared to the non - sarcopenic females. On the other hand, the rest of the parameters, such as mid - arm and thigh circumference, P. M area and hand grip strength, were significantly lower in sarcopenic vs non - sarcopenic females [18.94±2.22 vs 21.52±3.49; 35.00±5.02 vs 37.98±5.53; 4.87±0.47 vs 5.90±0.39]. A significant difference was noted in these clinical parameters among the patients. In sarcopenic males, the mean serum albumin was [2.70±0.32] significantly lower than in non - sarcopenic males [2.83±0.44]. The mean mid - arm and thigh circumference, PM area and hand grip strength were significantly lower in sarcopenic males than non - sarcopenic males. This was a similar pattern as we found in females. Similarly, MELD and Child - Pugh scores were higher in sarcopenic vs non - sarcopenic males [19.17±3.51 vs 11.44±2.70; 10.13±2.19 vs 6.22±0.83]. The presence of hand grip was higher among male patients, 83 (93.3%), than among females 6 (6.7%). Also, in the case of the absence ofhand grip, it was higher in males than females. The hand grip association in gender wise population was highly significant. Similarly, **Puri P et al.** [16] reported mean HGS in the non - cirrhotic Indian population was 25.19 ± 7.57 kg in females versus 35.14 ± 8.56 kg in males. We observed that 84.8% of the patients had a high frequency

of hand grip in the present study. Another study showed a correlation between HSG and fatality in cirrhotic patients. [2]The serum albumin [p= **0.004;** r=0.279;], mid - arm circumference [p=0.054; r= 0.189], mid - thigh circumference [p<**0.001;** r=0.960] and P. M area [p<**0.001;** r=0.788] were statistically significant and positively correlated with P. M Index in our study. On the other hand, there was a negative correlation between P. M Index vs MELD Score [p<**0.001;** r= - 0.595] and Child - Pugh Score [**p<0.001;** r= - 0.573]. No such correlation was observed between the P. M Index and the age of the patients [p=0.949; r=0.006]. The severity and prevalence of sarcopenia in cirrhosis correlate with theChild–Pugh score. [34] Further, we recorded a negative correlation between hand grip strength vs P. M index [r= - 0.019] and age [r= - 0.024], though it was insignificant. On the other hand, the MELD score [p<**0.001; r=** - 0.646] and the Child - Pugh score [p<**0.001;** r= - 0.560] were negatively correlated. Mid - thigh circumference [r=0.776] and P. M area [r=0.788] showed a significant positive correlation. There was no significant correlation between serum albumin and Mid - arm circumference with respect to hand grip strength.84.8% of the patients had a high frequency of hand grip. Evaluation and treatment of sarcopenia should be part of normal assessment for patients with chronic liver disease. To achieve best clinical outcomes, it is essential to advance interprofessional communication, pharmacological research, patient education, and patient adherence. Physical activity and nutrition modification are the most effective modalities to combat sarcopenia. To maximise the utility of this knowledge, doctors, dietitians, and physical therapists must collaborate to enhance patient outcomes.

5. Conclusion

Based on the findings of this study, we can say that anthropometric parameters are suitable for assessing nutritional status. MELD and the CTP score are excellent prognostic indicators for sarcopenia in CLD patients. It can deduce that a high frequency of sarcopenia in patients with CLD is related to worseclinical outcomes and a shorter survival rate. Identification of suspected sarcopenia gives a treatment efficacy during which early interventions would be advantageous and avert problems. Our study has a few limitations, such as it lacked randomization and blinding, which may have contributed to a degree of bias in case selection; also, the sample size was small (n=105), and follow - up time was not done to check the further impact of sarcopenia, and lastly, it was a single - centric. It may not be generalized for a larger population.

Consent:
The authors have collected and preserved written participant consent per international or university standards.

Ethical Approval:
The author (s) has collected and preserved written ethical permission per international or university standards.

References

[1] Morimoto RI, Cuervo AM. Proteostasis and the aging proteome in health and disease. Journals of Gerontology Series A: Biomedical Sciences and Medical Sciences.2014 Jun 1; 69 (1): S33 - 8.

[2] Musso G, Paschetta E, Gambino R, Cassader M, Molinaro F. Interactions among bone, liver, and adipose tissue predisposing to diabesity and fatty liver. Trends in molecular medicine.2013 Sep 1; 19 (9): 522 - 35.

[3] Liu J, Xu Y, Hu Y, Wang G. The role of fibroblast growth factor 21 in the pathogenesis of non - alcoholic fatty liver disease and implications for therapy. Metabolism.2015 Mar 1; 64 (3): 380 - 90.

[4] Sidhu SS, Saggar K, Goyal O, Varshney T, Kishore H, Bansal N, et al. Muscle strength and physical performance, rather than muscle mass, correlate with mortality in end - stage liver disease. European Journal of Gastroenterology & Hepatology.2021 Apr 1; 33 (4): 555 - 64.

[5] Meex RC, Watt MJ. Hepatokines: linking nonalcoholic fatty liver disease and insulin resistance. Nature Reviews Endocrinology.2017 Sep; 13 (9): 509 - 20.

[6] Evuri P, Caroline S, Manimekala E, Aravind A, Karunakaran P, Muthukumaran K, et al. Study of Prevalence of Sarcopenia in Chronic Liver Disease and its Impact on Outcomes. International Journal of Innovative Research in Medical Science.2022 July; 7 (7): 335 - 339.

[7] Montano - Loza AJ, Duarte - Rojo A, Meza - Junco J, Baracos VE, Sawyer MB, Pang JX, et al. Inclusion of sarcopenia within MELD (MELD - Sarcopenia) and the prediction of mortality in patients with cirrhosis. Clinical and translational gastroenterology.2015 Jul; 6 (7): e102.

[8] Ebadi M, Bhanji RA, Mazurak VC, Montano - Loza AJ. Sarcopenia in cirrhosis: from pathogenesis to interventions. Journal of gastroenterology.2019 Oct; 54 (10): 845 - 59.

[9] Kim G, Kang SH, Kim MY, Baik SK. Prognostic value of sarcopenia in patients with liver cirrhosis: a systematic review and meta - analysis. PloS one.2017 Oct 24; 12 (10): e0186990.

[10] Riggio O, Angeloni S, Ciuffa L, Nicolini G, Attili AF, Albanese C, et al. Malnutrition is not related to alterations in energy balance in patients with stable liver cirrhosis. Clinical Nutrition.2003 Dec 1; 22 (6): 553 - 9.

[11] Carvalho L, Parise ER. Evaluation of nutritional status of nonhospitalized patients with liver cirrhosis. Arquivos de gastroenterologia.2006; 43: 269 - 74.

[12] Ardeljan AD, Hurezeanu R. Sarcopenia. InStatPearls [Internet] 2022 Jul 4. StatPearls Publishing.

[13] Hanai T, Shiraki M, Nishimura K, Ohnishi S, Imai K, Suetsugu A, et al. Sarcopenia impairs prognosis of patients with liver cirrhosis. Nutrition.2015 Jan 1; 31 (1): 193 - 9.

[14] Meza - Junco J, Montano - Loza AJ, Baracos VE, Prado CM, Bain VG, Beaumont C, et al. Sarcopenia as a prognostic index of nutritional status in concurrent cirrhosis and hepatocellular carcinoma. Journal of clinical gastroenterology.2013 Nov 1; 47 (10): 861 - 70.

[15] Reddy YK, Maliakkal B, Agbim U. Nutrition in chronic liver disease. Current treatment options in gastroenterology.2019 Dec; 17: 602 - 18.

[16] Puri P, Dhiman RK, Taneja S, Tandon P, Merli M, Anand AC, et al. Nutrition in chronic liver disease: consensus statement of the Indian National Association for Study of the Liver. Journal of clinical and experimental hepatology.2021 Jan 1; 11 (1): 97 - 143.

Tables and Figures

Table 1: Demographics of enrolled patients (n=105)

Demographics		Mean/ N	SD/%
Age		41.69	9.93
Gender	Male	93	88.6
	Female	12	11.4

Table 2: Laboratory Investigations of enrolled patients (n=105).

Parameters	Mean	SD
Serum Albumin	2.70	0.32
Mid Arm Circumference	23.41	4.35
Mid - Thigh Circumference	37.39	6.46
Psoas Muscle Area	7.51	1.10
Psoas Muscle Index	4.74	0.67
Hand Grip Strength	22.19	3.39
MELD Score	18.54	4.18
Child - Pugh Score	9.81	2.42

Table 3: Hand grip among males and females (n=105).

Gender	Hand Grip						p - value
	Present		Absent		Total		
	N	%	N	%	N	%	
Male	83	93.3	10	62.5	93	88.6	p<0.0001*
Female	6	6.7	6	37.5	12	11.4	

Table 4: Sarcopenia in enrolled patients (n=105).

SARCOPENIA	N	%	p - value
Present	90	85.7	**p<0.0001***
Absent	15	14.3	
Total	105	100	

Table 5: Laboratory parameters with respect to sarcopenic males and females

SARCOPENIC MALES					
Parameters	Present		Absent		**p - value**
	MEAN	SD	MEAN	SD	
Serum Albumin	2.70	0.32	2.83	0.44	t=2.448 **p=0.0152***
Mid Arm Circumference	23.57	3.92	27.11	5.73	t=5.225 **p<0.0001***
Mid - Thigh Circumference	37.11	6.56	42.44	5.20	t=6.524

					p<0.0001*
Psoas Muscle Area	7.61	0.63	9.41	0.37	t=25.25 **p<0.0001***
Hand Grip Strength	22.10	2.72	28.00	2.78	t=15.54 **p<0.0001***
MELD Score	19.17	3.51	11.44	2.70	t=17.89 **p<0.0001***
Child - Pugh Score	10.13	2.19	6.22	0.83	t=17.11 **p<0.0001***
SARCOPENIC FEMALES					
Serum Albumin	2.65	0.25	2.55	0.19	t=3.263 **p=0.0013***
Mid Arm Circumference	18.94	2.22	21.52	3.49	t=6.392 **p<0.0001***
Mid - Thigh Circumference	35.00	5.02	37.98	5.53	t=4.089 **p<0.0001***
Psoas Muscle Area	4.87	0.47	5.90	0.39	t=17.28 **p<0.0001***
Hand Grip Strength	17.50	2.26	19.33	1.37	t=7.095 **p<0.0001***
MELD Score	20.50	5.58	17.44	3.73	t=4.672 **p<0.0001***
Child - Pugh Score	11.24	3.02	8.98	2.53	t=5.878 **p<0.0001***

Table 5: Correlation of PM index and Hand grip strength with other investigations of enrolled patients

| Spearman Correlation		Correlation Coefficient	Sig. (2 - tailed)
Spearman Correlation of PM Index	P. M Index	1	
	Hand Grip Strength	0.006	0.949
	Age	0.107	0.279
	S. Albumin	.279**	**0.004**
	Mid Arm Circumference	0.189	**0.054**
	Mid - Thigh Circumference	.960**	**<0.001**
	P. M Area	.788**	**<0.001**
	MELD Score	- .595**	**<0.001**
	Child - Pugh Score	- .573**	**<0.001**
Spearman Correlation of Handgrip Strength	Hand Grip Strength	1	
	P. M Index	- 0.019	0.845
	Age	- 0.024	0.807
	S. Albumin	0.079	0.421
	Mid Arm Circumference	0.107	0.278
	Mid - Thigh Circumference	.776**	**<0.001**
	P. M Area	.788**	**<0.001**
	MELD Score	- .646**	**<0.001**
	Child - Pugh Score	- .560**	**<0.001**
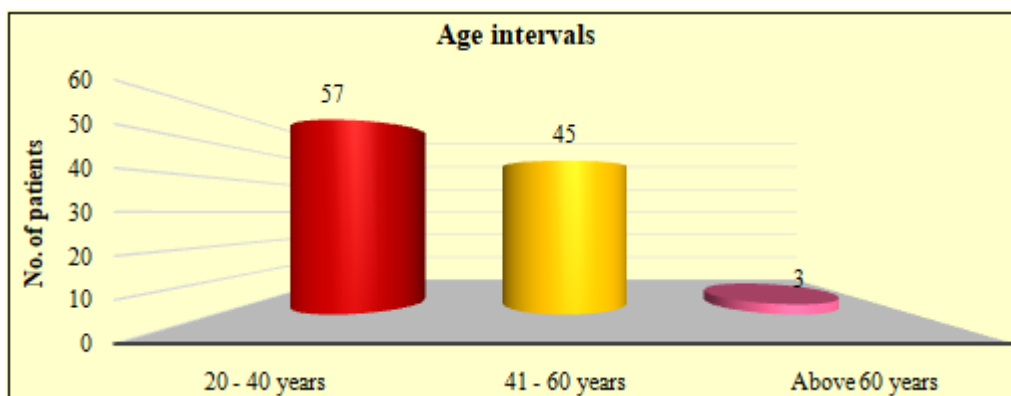
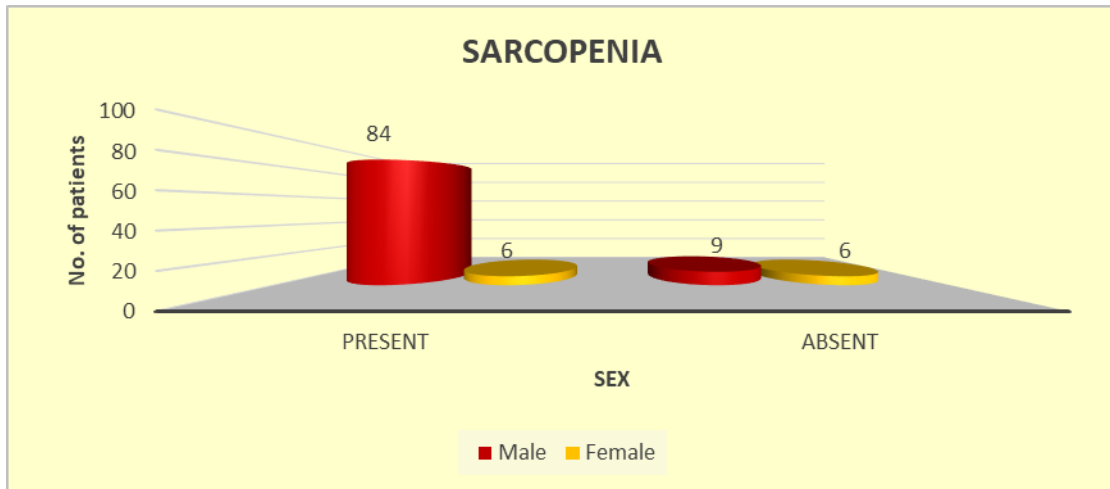**Figure 1:** Age - wise distribution of enrolled patients

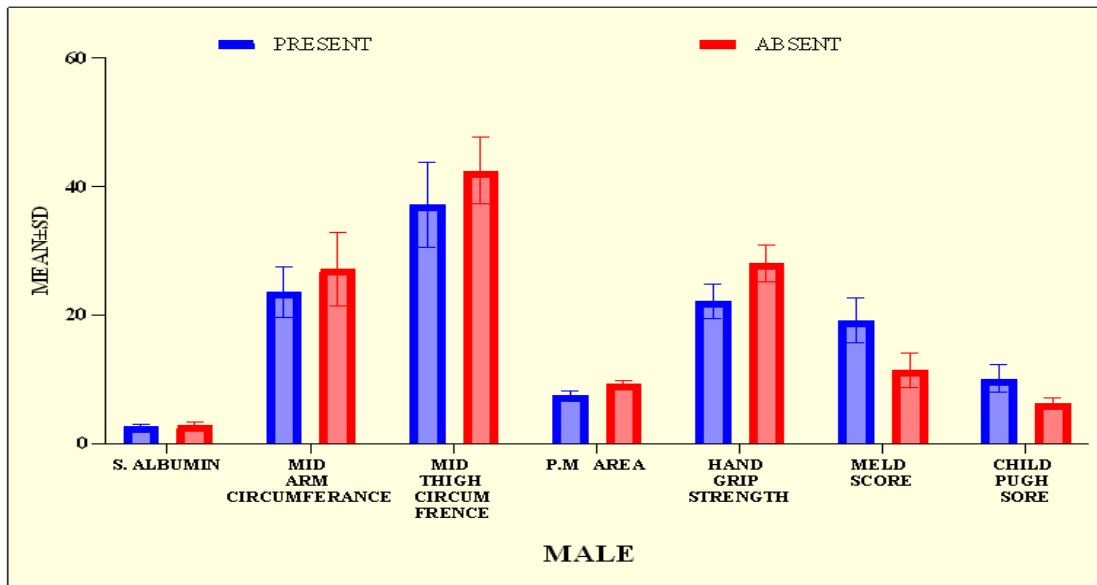**Figure 2:** Gender of sarcopenic patients.

Figure 3: Laboratory parameters of sarcopenic males.
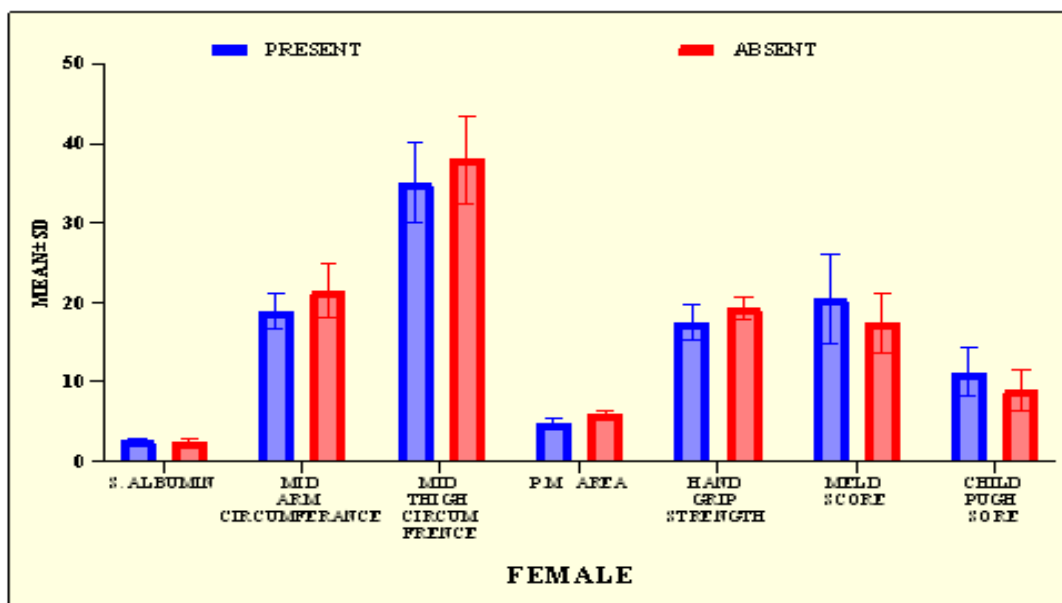

Figure 4: Laboratory parameters of sarcopenic females.
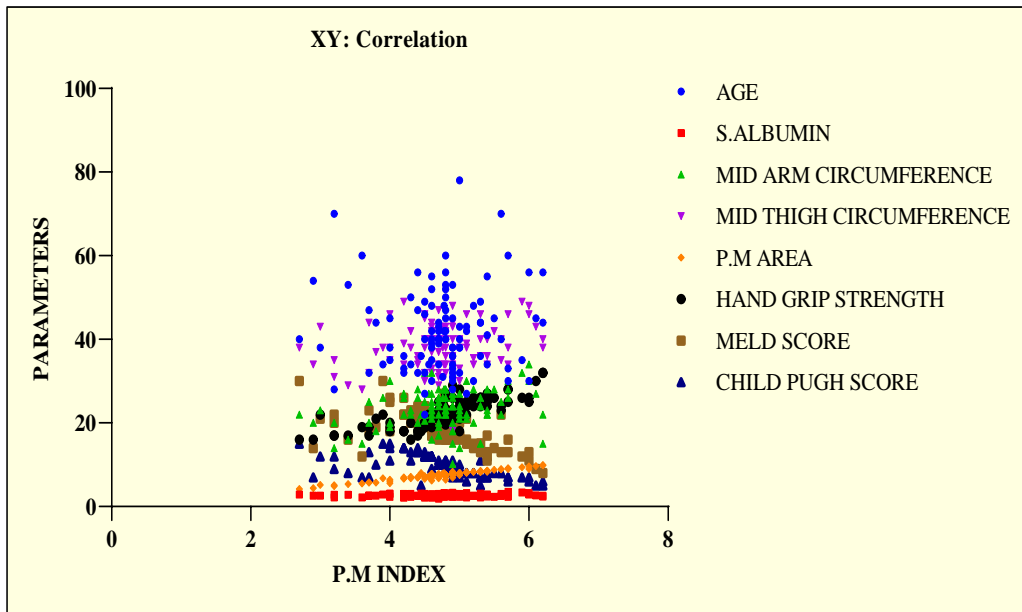
Figure 5: Correlation of PM index and other investigations of enrolled patients.

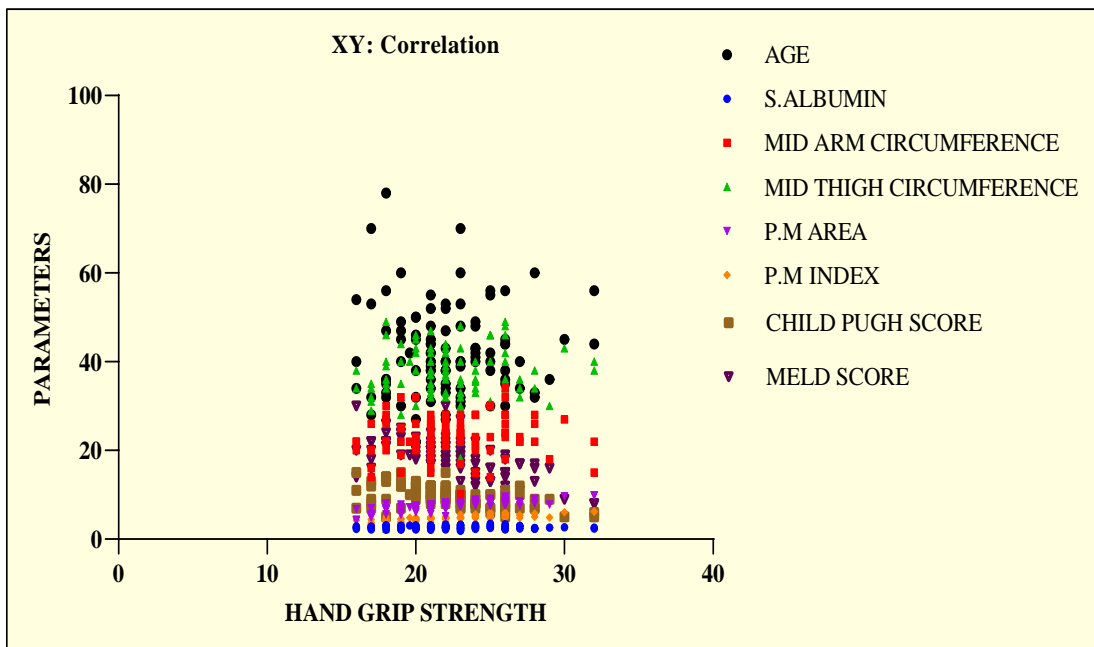**Figure 6:** Correlation of hand grip strength and other investigations of enrolled patients