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RESEARCH ARTICLE

A Study to Estimate the Prevalence of Sarcopenia in Chronic Pancreatitis

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Abstract

Background and Introduction: As an inflammatory disease with exocrine and endocrine insufficiency that resultantly leads to malnutrition and sarcopenia, Chronic Pancreatitis (CP) is associated with significant morbidity that drastically reduces the quality of life. While limited studies on CP in India indicate its widespread prevalence, the burden of CP and the associated sarcopenia in the regional Tamil Nadu population does not prevail. This study, conducted in urban Tamil Nadu at three tertiary-level centres, is the first regional investigation aimed at assessing the prevalence of sarcopenia in CP patients and the influence of age, gender, BMI, and associated causes/complications of CP on sarcopenia. **Methods:** A total of 160 patients diagnosed with CP and admitted to the MGE ward of Government Kilpauk Medical College, Government Peripheral Hospital Anna Nagar, and Government Royapettah Hospital between March 2024 and September 2024 were included in the study. Sarcopenia in the CP patients was diagnosed using Computed Tomography (CT) of the abdomen to assess the Psoas Muscle Index (PMI). **Results:** The study identified a 1.6% prevalence of CP in the assessed regional population, with 160 patients among 10,000 individuals. Of these, 16% were female, and 84% were male. The PMI values significantly varied across the underweight, normal, and overweight BMI categories of the CP patients. Sarcopenia was prevalent in 46% of the CP patients, among which 52% of the patients were male and 15% were female. The PMI values differed significantly based on gender between males and females and based on age, in the age category 66-85, between the sarcopenic and non-sarcopenic groups, and were associated with sarcopenia. The PMI values between the sarcopenic and non-sarcopenic groups varied significantly, and 47% of the CP patients in the ideal weight category were sarcopenic. Further, the results indicated that complications such as diabetes mellitus (47%), exocrine pancreatic insufficiency (14.4%) and cirrhosis (11.9%) were significantly more prevalent among sarcopenic patients. The results also revealed that DM is associated with sarcopenia in the present study. The percentage of patients with alcoholic and smoking aetiology in the sarcopenic group was 14.9%, and smoking 17.6%, and did not contribute as a major population among the sarcopenics. Taken together, the results reveal that sarcopenia is widely prevalent in the CP study population, and age, gender, and BMI categories had significantly varying PMI between the sarcopenic and non-sarcopenic groups. **Conclusion:** The study, as a first initiative, underscores the critical role of sarcopenia in CP disease progression and highlights the importance of early diagnosis with PMI and CT. The study underlines the need for targeted interventions, including nutritional and lifestyle modifications, to improve patient outcomes, thereby laying the foundation for future multicentric research that would address the complications of CP in diverse populations.

Keywords: Chronic Pancreatitis, Diabetes Mellitus, Exocrine Insufficiency, Psoas Muscle Index, Sarcopenia

1. Introduction

Irreversible destruction of the pancreatic tissue owing to recurrent Inflammatory episodes with characteristic clinical and morphological features such as pancreatic fibrosis, parenchymal/intraductal calcification and endocrine, exocrine pancreatic insufficiency, is typically defined as CP. Resultantly, patients with chronic pancreatitis suffer from malabsorption, diabetes, cirrhosis and susceptibility to pancreatic cancer.

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Such severe complications in CP patients drastically decrease the quality of life, increase hospitalisations, and predict poor disease prognosis[1,2]. Further, recent studies have also brought to light that risk factors in the incidence of CP are multi-factorial, among which alcoholism and smoking/tobacco usage are considered to be predominant risk factors. Additionally, about 20% of the CP patients are idiopathic[3] and about 5-10% of the aetiology is attributed to genetic causatives. Physiological/molecular mechanisms that drive CP are inclusive of the activation of proteases, ductal dysfunction-related mechanisms, and endoplasmic stress-related mechanisms[4]. Differences in etiologies, causative factors, clinical presentations at the time of the diagnosis and research study limitations, such as selective recruitment is reported to prevail across the globe in CP. Therefore, it becomes critically necessary to understand the regional prevalence of the disease and its complications, for better management of the disease[5]. Western, industrialised nations tend to exhibit a higher prevalence of CP, in particular alcoholic CP[3], while CP patients from India tend to exhibit more of an idiopathic nature. Earlier reports from South India had reported that the prevalence of CP in India was higher, with about 11.4-20 in 10000 popula[6]. A majority of the prevalence studies in CP are specific to populations, and several region-specific prevalence studies that are required for better treatment strategies are not available in India/Tamil Nadu.

Sarcopenia, which is a resultant complication in CP, serves as an independent factor that relates to increased hospitalisation, poor surgical outcomes, poor prognosis and mortality[7,8]. The persistence of a pro-inflammatory state, exocrine insufficiency and malnutrition are primarily recognised for the development of sarcopenia in CP patients[9]. Sarcopenic CP patient risk for mortality is significantly high (16%) when compared to the non-sarcopenics, that attributes to about 3% only[10]. Although sarcopenia is observed to be widely prevalent across the globe in a range accounting to 17-62%[11], understanding its prevalence in the regional population becomes critical for preventing disease progression and enabling better treatment strategies. Poor muscle quantity and quality, physical inability, portray sarcopenia and are reflective of CP prognosis. The Psoas major muscle cross-sectional area (PMI) is utilised to understand overall muscle mass, and the cross-sectional view of the psoas muscle using CT is demonstrated to enable estimation of the lean muscle mass[8,12]. Owing to the difference in muscle mass between the healthy patient population and the male and female populations, consensus documents that emphasise cutoff values have been used as standard references[11] to precisely diagnose sarcopenia.

Age and gender are important factors that influence muscle mass and muscle function that pertain to sarcopenia diagnosis[13]. Of note, the aetiology of sarcopenia in the south Indian population and the association of gender, age, and BMI in sarcopenia is also not known in the Tamil Nadu population. Similarly, in terms of the percentage prevalence of CP nonalcoholic/idiopathic, genetic association data, alcoholic smoking habits are lacking in India/south India. Since there exists a huge lacuna in understanding the prevalence of sarcopenia and the influence of other etiological factors in the regional CP patients of Tamil Nadu, the present study aimed to address these concerns.

2. Aims and Objectives of the Study

2.1 Aims

This study aims to estimate the prevalence of sarcopenia in chronic pancreatitis.

2.2 Objectives

- To estimate the prevalence of sarcopenia in chronic pancreatitis
- To analyse the influence of
  - Gender, age, BMI
  - Alcoholic, smoking habits, and
  - Complications of CP, such as exocrine insufficiency and DM in the sarcopenic and non-sarcopenic CP patients

3. Materials and Methods

3.1 Study Design

This study was a cross-sectional observational study conducted to evaluate the prevalence of sarcopenia and its associated complications in patients diagnosed with CP.

3.2 Patient Selection

Patients were recruited from three government healthcare institutions in Chennai, Tamil Nadu, where

they were admitted to the Medical Gastroenterology (MGE) wards. Eligible patients were those diagnosed with CP based on clinical, radiological, and laboratory findings. The diagnosis of chronic pancreatitis was made using Endoscopic Ultrasound (EUS) in accordance with the Rosemont criteria for imaging-based identification of CP. The Rosemont criteria include both major and minor criteria based on EUS findings. Chronic pancreatitis was diagnosed when at least one major criterion and/or two minor criteria were met, in line with the Rosemont criteria, as described earlier.

EUS diagnosis of CP on the basis of Rosemont criteria.

I. Consistent with CP
A. 1 Major A feature + ≥3 minor features
B. 1 Major A feature + major B feature
C. 2 Major A features
II. Suggestive of CP
A. 1 Major A feature + <3 minor features
B. 1 Major B feature + ≥3 minor features
C. ≥5 Minor features (any)
III. Indeterminate for CP
A. 3 to 4 Minor features, no major features
B. Major B feature alone or with <3 minor features
IV. Normal
≤2 Minor features, no major features

Source : Reference 11

3.3 Time Period

The study was carried out over six months, from March 2024 to September 2024.

3.4 Sample Size

A total of 160 patients were included in the study, determined by the expected prevalence of sarcopenia in CP patients and the available patient population during the study period.

3.5 Data Collection

Upon obtaining informed consent, all eligible patients underwent a CT scan of the abdomen to assess skeletal muscle mass using the PMI. The PMI was measured at the level of the third lumbar vertebra (L3), and the area of the bilateral psoas muscles was quantified. The psoas muscle area was normalised for body size by dividing the total cross-sectional area by the square of the patient's height (in centimetres). The cut-off values for diagnosis of sarcopenia using PMI were taken as 5.4 cm/mm^2 for males and 3.6 cm/mm^2 for females[14].

In addition to imaging, patient demographic data (age, sex, BMI), clinical history (including smoking and alcohol use), and conditions (such as diabetes and cirrhosis) were collected through structured interviews and medical record reviews.

3.6 Outcome Variable

The primary outcome variable was the PMI, which was used to diagnose sarcopenia. The PMI was calculated by measuring the cross-sectional area of the psoas muscles at the L3 vertebra using CT scans. This measure was then adjusted for individual height to derive the muscle index, which was compared across different groups of patients. The PMI cut-off values were based on established guidelines and relevant literature.

3.7 Statistical Analysis

Data were entered into Microsoft Excel and cleaned before analysis. The statistical analysis was performed using SPSS software (version 23). Descriptive statistics were used to summarise continuous variables, which were presented as means with Standard Deviations (SD) as appropriate. Categorical data were presented as frequencies and percentages.

Comparative analyses between categories/ groups were performed using Student's t-test for continuous variables. Chi-square (χ^2) tests were used to compare categorical variables. To evaluate differences in PMI across different BMI categories, ANOVA (Analysis of Variance) was used. If significant differences were found, Tukey's test was applied to identify which specific groups were different from each other. Pearson's correlation coefficient was employed to evaluate the relationship between BMI and PMI. A p-value of <0.05 was considered statistically significant.

3.8 Ethical Considerations

The study was approved by the ethics committees of the participating hospitals. All participants provided written informed consent before their inclusion in the study.

4. Review of Literature

Chronic pancreatitis, defined as a *pathologic fibroin flammatory syndrome of the pancreas, is attributed to genetic, environmental, and socio-cultural risk factors in susceptible individuals, leading to a persistent, abnormal response to pancreatic parenchymal injury/ stress*. This recent definition is inclusive of risk factors,

disease progression and biomarkers, and the variables attributable during the disease progression. The relentless progression of the disease culminates in duct distortion and strictures, calcifications, pancreatic exocrine as well as endocrine insufficiency, dysplastic changes, constant significant pain, fibrosis and pancreatic atrophy[15].

Acute and chronic pancreatitis, pancreatic cancers exhibit more or less similar pathological changes. The hallmark of CP is the end-stage pancreatic atrophy, causing significant Pancreatic Exocrine Insufficiency (PEI). PEI leads to fat malabsorption with symptoms like pain, bloating, diarrhoea, micronutrient deficiency and progressive severe malnutrition[3,15]. Since morbidity in CP patients is significantly high, and strategies for the management of sequlae of complications arising from exocrine and endocrine insufficiency of CP[16] and necessary measures such as behavioural modifications, endoscopic measures, surgical interventions are required to be a part of the management plan.

Causatives for CP are primarily inclusive of alcoholism, tobacco use, usage of drugs which are toxic to the organ, specific viral infections, abnormal pancreatic or biliary architecture, gallstone predisposition, and autoimmune conditions that may cause irreversible damage in the pancreas. Recent studies bring to light that CP and the associated sarcopenia are caused by Multi-factorials rather than single causatives[1,2]. Further, premature activation of pancreatic proteases that causes acinar injury, stress-related injury of the endoplasmic reticulum of the pancreatic acini are also attributed to the incidence of CP. Recurrent episodes of acute pancreatitis, which are usually caused by environmental and social risk factors, are also reported to lead to CP. Interesting evidences indicate that smoking and drinking increase the risk of incidence of CP by 18%, 30%, respectively, and that cessation of drinking and smoking reduces the risk of CP substantially[17,18]. Alcoholic habits induce pancreatic acinar injury by the production of oxidative, non-oxidative metabolites and further cause ischemia of acini, thereby triggering an inflammatory cascade that culminates in necro-inflammatory response and fibrosis[19].

Genetic susceptibility factors and disease-modifying mutations in conjunction with environmental/behavioural risk factors also contribute to the pathology progression in the category of idiopathic CP[20]. The PRSS1 gene with autosomal dominance has been strongly linked with hereditary pancreatitis, CPA1 and CEL, CTFR, which lead to ductal distortion and acini injury, are some mechanisms of injury[3].

Understanding the prevalence of CP in the regional population/geographical location as the paradigm of the disease includes advancement in stages that are irreversible. As such, there has been no cure for the recurrent episodes of severe abdominal pain/complications, and therefore, it becomes vital to continuously monitor and manage the disease in the best possible manner. Common observations regarding CP also frame its wide prevalence across the globe and the varied clinical presentation. Such differences in the clinical stages, presentation and therefore the treatment modalities are attributed to alcoholic, smoking and idiopathic etiologies. A majority of the studies on CP pertain to a specific population and other specific selection criteria.

Recent years have brought to light an increase in the prevalence of CP that can be linked to industrialisation, exposure to xenobiotics, and excess production of free radicals. Even though alcoholic CP in the western world is high, and a daily alcohol intake of >80g /day for at least 5 years[21] induces CP, the prevalence of CP in South India is higher compared to the western world, with an average of 11-200 per 100000 population. However, of late, alcohol induced CP is showing a declining trend, whereas a higher prevalence is noted in South Asian countries apart from other etiological causes[22]. Studies comparing the global burden of alcoholic pancreatitis between the East and West indicate that France presented with a prevalence of around 83% when compared to 64% for Korea and 68% for Japan, respectively. In contrast, recent studies from USA, Italy and Hungary demonstrate that only 50% of the patients had alcoholic pancreatitis.

CP patients are aged between 40 and 62 years on average, and about 5-10% of CP incidence is attributed to genetic/autoimmune conditions[5,23]. Idiopathic CP, which contributes to about 20% of the CP population in India, presents a mean age of onset of 40 years in India, when compared to 62 years in Japan. However, a contrasting study from the US reported that about 69% of the idiopathic CP patients had a late onset[22,24].

Idiopathic CP also shows a strong association with mutations like SPINK1 or CTFR polymorphisms.

A U.S based study carried out in 2001-2013 showed a widely varying prevalence between 25.4-98.7 % per 100,000 population, with 4-5 new cases per 100.000 per year, with slightly male preponderance and in the peak age group of 46-55 years. Another US registry-based analysis published in 2019 showed that pancreatitis is one of the three common benign GI diseases, with an emergency room visit of 12%. Similar studies carried out in China, Italy and Spain showed a prevalence between 13.5 and 52.4 cases per 100,000 and an incidence of five new cases per 100,000 per year[25-27]. The North American Pancreatitis Study 2 and the North American Pancreatitis continuation and validation study 2 are two notable studies clearly depicting the demographic trends of CP. Contrary to the belief that CP predominantly involves middle-aged individuals with ethanol abuse, the studies established that the CP cohort is diverse. It has been documented that genetic susceptibility causes a significant contribution in non-whites compared to the white population, and further studies are warranted to evaluate social inequity in genetically susceptible non-white populations[24].

In the study cohorts of West Vs East, systemic and local complications were found to be similar; Malabsorption, diabetes in one third of patients and biliary stricture in one fourth of patients were also similar, but pancreatic pseudocysts and cancer occurrence were more prevalent in Western cohorts[5]. Other important studies have also demonstrated that CP is associated with accelerated biological aging and the life span is reduced by 8 years in a cohort with matched age and gender[28]. In the course of pathological progression in the South Korean alcoholic CP patients associated with diabetes, pseudocysts[29], however, such in-depth studies that assess the relevance of specific etiologies to the development of complications, long-term prognosis are lacking in several other countries, as well as in India.

Of major concern are the results from findings that have demonstrated that 30-50% of the CP patients have an increment in resting energy expenditure[30], and the intractable pain, alcoholism, malabsorption, and maldigestion due to pancreatic exocrine insufficiency boogle down to contribute to the risk of incidence of sarcopenia in CP patients.

In yet another dimension, studies pertaining to obesity and CP indicate that CP patients who were overweight/obese displayed micronutrient deficiencies and lower muscle strength, capacity[31]. In CP patients with metabolic syndrome, pancreatic steatosis and hypertriglyceridemia have been reported, and another retrospective study had indicated that high visceral fat correlated with high levels of pancreatic fat. However, in other studies, it was observed that about 33% of CP patients were diabetic and obese[32]. Micro and macro levels of the architecture, composition of the muscle is impaired in sarcopenia[33].

Sarcopenia is defined when low muscle quantity or quality is confirmed and severe enough, with low muscle strength and poor physical fitness. It can be primary when loss in muscle mass and muscle strength is not associated with any other cause other than ageing itself; Secondary when loss of muscle mass and strength is associated with underlying chronic disease, malignancy and malnutrition. CP patients with pancreatic exocrine insufficiency have been documented with sarcopenia and low serum albumin levels. Conventionally, muscle tissue loss commences at 40 years and progresses at 8% every 10 years until 70 years and then accelerates to 15% every decade. Sarcopenia has a prevalence of 17-64% in CP patients as reviewed in this study. In CP patients with more than 50% pancreatic fibrosis, sarcopenia has shown to have a statistically significant negative impact on outcomes like lower quality of life, hospitalisation burden, mortality and lower islet cell yield following TPIAT. The attributable factors for sarcopenia are reduced caloric consumption, muscle fibre denervation, oxidative stress, hormonal imbalance and augmented myostatin signalling[34,35]. Furthermore, pre-existing comorbidities themselves may lead to loss of muscle mass and an escalation in the adverse events associated with sarcopenia in CP.

Risk factors that precipitate sarcopenia in CP also include malnutrition owing to abdominal pain and the early disease course before the diagnosis of PEI. Other associated factors are Opioid treatments. Earlier studies have also clearly indicated that sarcopenia is more prevalent in patients with PEI and attributes to about 67%, while patients without PEI presented with only about 37%. Similarly, the prevalence of sarcopenic obesity was also higher in the PEI group of CP patients. Sarcopenic obesity is indicated by a

reduction in lean body mass in the context of excess fat and is easily overlooked in obese patients. Of note, both sarcopenia and sarcopenic obesity were significantly associated with pancreatic exocrine insufficiency regardless of pathological changes in CP, and such patients had increased morbidity and mortality. Additionally, diabetes and sarcopenia are demonstrated to be independently associated with pancreatic insufficiency[36].

Conventional anthropometric parameters have a low index in detecting sarcopenia and do not provide for an accurate assessment of muscle tissue[37]. The same applies to the conventional nutritional assessment. Radiology has proven to be more reliable in the examination of body composition with a high degree of differentiation between muscle and fat, as well as the distribution of adipose tissue within intermuscular, subcutaneous and visceral sites[34]. DEXA scans (Dual energy X-ray absorptiometry scan) are non-invasive, inexpensive, accurate and regarded as the ideal standard for quantification of muscle mass. However, the gold standard for non-invasive measurement of muscle mass is Magnetic Resonance Imaging (MRI) and CT[10]. In contrast to MRI, CT is faster, more widely accessible, and cheaper. Radiation exposure of arms or legs is low (<0.5 mSv), while volumetric muscle measurements of the trunk are associated with higher exposure, with an annual background radiation of about 2.5 mSv. One advantage of CT is the possibility to quantify the muscle density, also termed as muscle attenuation or muscle radiation attenuation, which linearly depends on the muscle fat content. The muscle volume may be measured either with MRI or CT. However, the spatial resolution of CT images is higher. Typical MR parameters are a slice thickness of 3 mm and an in-plane pixel size of 0.5 mm, whereas for CT, a slice thickness of 1 mm and an in-plane pixel size of 300 microns are state of the art[38]. The cross-sectional area of the Psoas major muscle measured using CT enables understanding muscle capacity (mass, volume) and predicting lean muscle mass. It provides distinct cutoffs that would be interpretive of age, gender and conditions such as sarcopenia[39].

The objective and precise assessment of sarcopenia/sarcopenic obesity using CT data was introduced in 2013, but the cutoff points were arbitrary. Prado et al defined sarcopenia cut-offs at approximately 52.4 cm^2/m^2 for men and 38.5 cm^2/m^2 for women[14]. This, however, did not reflect the junctional muscle status[7] did a comparative study of patients with CP and pancreatic ductal adenocarcinoma with regard to sarcopenia was conducted, and reported that a substantial number of cases of sarcopenia were detected in patients with CP (62%), clearly demonstrating that sarcopenia was more often associated with chronic diseases in contrast to malignancy[7]. A similar potentially confounding variable was derived with the study of 58, where all pancreatic pathologies (malignancy, neuroendocrine and CP) were analysed separately in subgroups.

Studies investigating the influence of BMI and sarcopenia in CP/non-CP patients demonstrate that, irrespective of underweight, overweight, or normal weight, sarcopenia is prevalent in CP patients. Such studies have also highlighted that different percentages of lean and adipose tissue could be observed even in individuals with similar BMI[14]. Further studies on sarcopenic patients have also indicated that about 74% of the sarcopenic patients' BMI can range between the normal/ideal weight range and the obese weight range[39]. Other studies have also demonstrated a significant association for sarcopenia among the BMI subgroups[40].

Taking into account that there is a paucity of research focusing specifically on sarcopenia in CP patients, and that there prevails major heterogeneity in the outcomes of sarcopenia related results, and the fact that in a complex disease like CP, an optimal body habitus and reversal of sarcopenia is unlikely to be achievable in short term[34], population specific studies in CP patients with sarcopenia are required for the benefit of patient specific therapeutic strategies. Taking this into account, the present study focused on estimating the prevalence of sarcopenia in CP patients from Chennai, Tamil Nadu. Further, large cohort studies will shed more light on the aetiology, the successful implementation of the current treatment modalities and prevention strategies.

5. Results

Sarcopenia associated with CP is of major concern and requires early intervention as it negatively impacts outcomes in CP patients, severely limiting quality of life. Patients with CP and sarcopenia experience a great degree of pain, work impairments, higher level of expenditure, malnourishment, anxiety and depression[41].

Understanding the prevalence of CP, its aetiology shares knowledge for making appropriate interventions and policies. In the south Indian scenario, particularly Tamil Nadu, there exists a paucity of data regarding the prevalence of sarcopenia in CP patients, and, therefore, the present study focused on estimating the prevalence of sarcopenia in CP patients from Government Kilpauk Medical College, Government Peripheral Hospital, Anna Nagar and Government Royapettah Hospital, Chennai, Tamil Nadu, India. In order to estimate the prevalence of sarcopenia, the present study calculated PMI using computerised tomography.

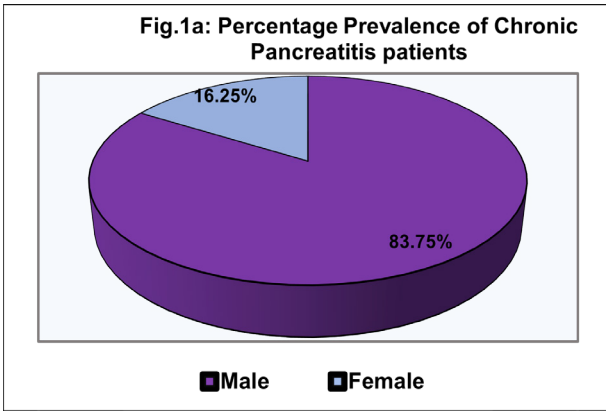
Table 1 presents the mean values, range for age, height, weight, BMI and PMI in the CP patients. The prevalence of CP accounts to 1.6% in the assessed regional population (160 patients in about 10000 people), and as indicated in Figure 1(a), among the CP patients, about 16% were females and 84% were males.

Figure 1(b) presents the mean±SD in the male and female CP patients, and it can be observed that the mean PMI in males was 5.77±1.57 and in females was 5.68±1.83. Table 2 presents the percentage prevalence of CP patients in various age categories (20-45, 46-65, 66-85) in complications of CP, such as cirrhosis, DM, exocrine insufficiency, habits such as smoking, drinking and in the underweight, normal, and overweight BMI categories.

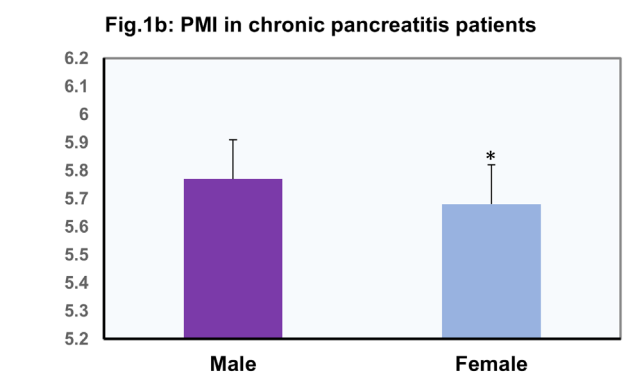
In order to understand the distribution of PMI across the BMI categories, we analysed the data in the male and female CP patient population. Figure 2, Table 3 presents the PMI mean±SD for the underweight, normal and overweight categories. It can be observed that the PMI values ranged from a minimum of 3.64 to 6, and significant differences in the PMI among the groups were assessed using the ANOVA test. As the table indicates, significant differences in the PMI values were noted among the groups ($p<0.001$). Subgroup analysis using a Tukey test

Table 1. Anthropometric parameters and PMI in CP patients

Variables	Mean	SD	Range
Age (years)	52	± 12.8	24-83
Height (cm)	162.1	± 7.5	140-178
Weight (kg)	54.2	± 7.1	40-72
BMI	20.71	± 2.8	14.3-27.1
PMI	5.75	±1.6	2.15-10



(a)



(b)

Figure 1. **(a)** Percentage prevalence of chronic pancreatitis patients, **(b)** PMI in chronic pancreatitis patients.

Table 2. Descriptive statistics for categorical variables

Variables	Criteria	Number	Percentage (%)
Age group	Below 45 years	58	36.2
	46-65 years	78	48.8
	Above 65 years	24	15
Diabetes Mellitus	Yes	75	46.9
	No	85	53.1
Exocrine insufficiency	Yes	23	14.4
	No	137	85.6
Alcoholic	Yes	21	13.1
	No	139	86.9
Smoker	Yes	25	15.6
	No	135	84.4
BMI categories	Underweight	39	24.4
	Ideal	86	53.7
	Overweight	35	21.9
Sarcopenia	Yes	74	46.25
	No	86	53.75

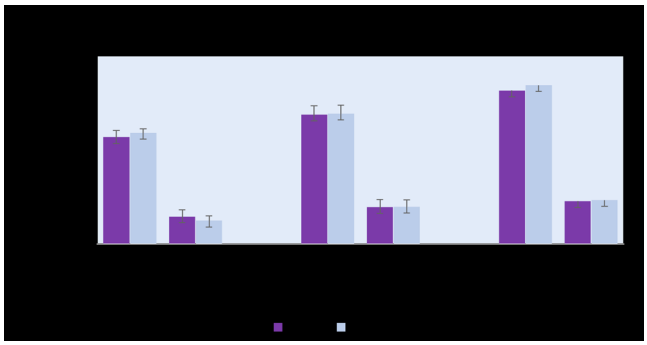


Figure 2. BMI and PMI in chronic pancreatitis patients.

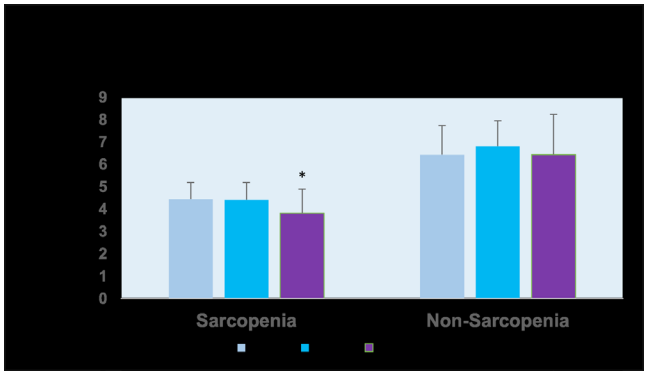


Figure 3. PMI and age in sarcopenic and non-sarcopenic CP patients.

Table 3. Comparison of PMI scores with BMI categories

BMI categories	Number	Mean	SD	pvalue[A]
Underweight	39	4.3	±1.13	<0.001
Ideal	86	5.94	±1.4	
Overweight	35	6.8	±1.5	

A - ANOVA

Subgroup comparison	pvalue[T]
Underweight vs. Ideal	0.003
Underweight vs. Overweight	0.001
Ideal vs. Overweight	0.025

T-Tukey test; p<0.05

also indicated significant differences in BMI across the categories.

The prevalence rate of sarcopenia among the CP patients is best estimated using techniques that can reliably reflect muscle quantity, quality and based on the earlier references, the present study used CT for measuring the PMI, and utilised 5.4 cm^2/m^2 in males and 3.6 cm^2/m^2 for females as a cutoff to diagnose sarcopenia[9]. As indicated in Table 4, it can be observed that sarcopenia was prevalent in 46% of the CP patients, among which 52% of the patients were male, and 15% were female.

Table 4. Prevalence of sarcopenia in CP patients

Gender	Prevalence		
	Number	Total	Percentage (%)
Male	70	134	52.2
Female	4	26	15.4
Total	74	160	46.2

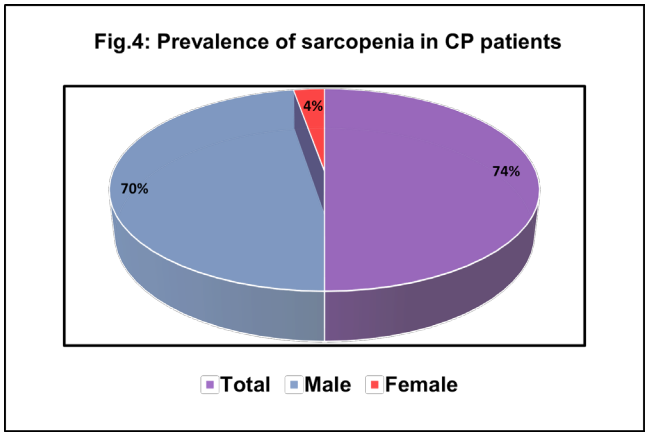


Figure 4. Prevalence of sarcopenia in CP patients.

The incidence of CP in males is more than in females, has been reported in several earlier studies, and that independent of age, a greater proportion of the sarcopenic CP patients were males[42].

Therefore, in the present study, we carried out a Chi Square statistical analysis that would enable determining the association between the variables, male/female and sarcopenia. As observed from Table 5, sarcopenia was significantly associated with the male gender (p<0.001)

As another important factor, age is identified to influence the incidence of chronic pancreatitis[4], and in relevance, the present study further focused on analysing the influence of age in sarcopenic CP patients.

Figure 3, Tables 6, 7 present the data for the PM index in the categorised age (20-45, 46-65 and 66-85) groups. As can be observed in Figure 3, the PMI values in the sarcopenic and non-sarcopenic groups differed significantly in the age group of 66-85 (p<0.001), and

Table 5. Association between Sarcopenia and Gender in CP patients

Gender	Sarcopenia		Non-sarcopenia		Total		pvalue[C]
	Number	Percentage (%)	Number	Percentage (%)	Number	Percentage (%)	
Male	70	94.6	64	74.4	134	83.7	**0.001**
Female	4	5.4	22	25.6	26	16.3	
Total	74	100	86	100	160	100	

Chi-square test; p<0.05 significant

Table 6. Association between sarcopenia and age categories

Age categories	Sarcopenia		Non-sarcopenia		Total		pvalue[C]
	Number	Percentage (%)	Number	Percentage (%)	Number	Percentage (%)	
Below 45 years	36	48.6	22	25.6	58	36.3	**0.009**
46 to 65 years	30	40.5	48	55.8	78	48.7	
Above 65 years	8	10.8	16	18.6	24	15	
Total	74	100	86	100	160	100	

Chi-square test; p<0.05 significant

Table 7. Correlation between age and PMI in sarcopenic and Non-sarcopenic CP patients

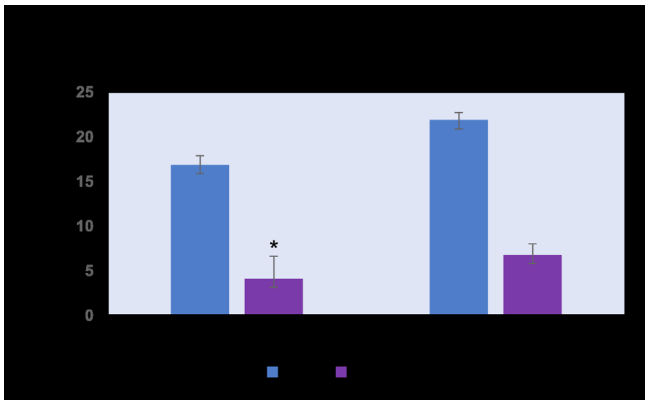
Age in years vs. PMI	Number	Correlation coefficient (r)	pvalue[P]
Sarcopenia group	74	-0.142	0.98
Non-sarcopenia group	86	0.22	0.99

P - Pearson correlation test; p<0.05 significant

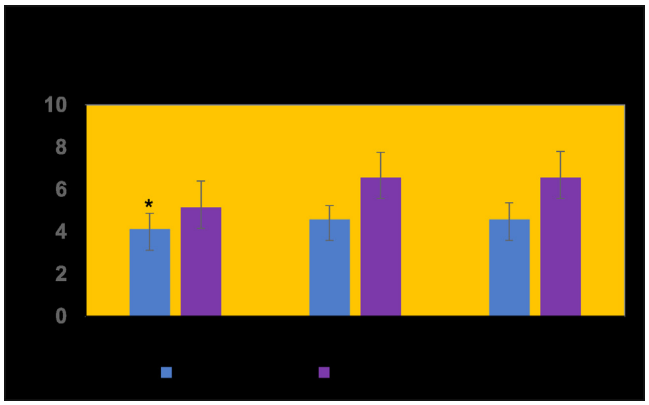
across the age categories when tested with a Chi-square analysis (p<0.001)

We further assessed if age correlated with the PMI in the sarcopenic and non-sarcopenic groups using Pearson's correlation analysis, and it can be observed that (Table 7) age significantly correlated with PMI, indicating that pathogenic progression in CP, in the present study, did not correlate with age.

Earlier reports have also documented that sarcopenic CP patients with a high body fat percentage and low BMI exhibit a negative life prognosis[9,40] and a low quality of life. In order to further understand the influence of BMI in sarcopenia, the study looked in detail into the BMI and PMI in the sarcopenic and non-sarcopenic groups (Figure 4a). Figure 4b presents the PMI across various categories of BMI. It can be observed that the Student's t-test brought to light that the PMI values varied significantly in the sarcopenic group and the underweight sarcopenic group (p<0.001).



(a)



(b)

Figure 4. **(a)** BMI and PMI sarcopenic and non-sarcopenic CP patients, **(b)** PMI in the sarcopenic and non-sarcopenic CP patients.

Table 8. Association between Sarcopenia and BMI

BMI categories	Sarcopenia		Non-sarcopenia		Total		pvalue[C]
	Number	Percentage (%)	Number	Percentage (%)	Number	Percentage (%)	
Underweight	33	44.6	6	7.0	39	24.4	**<0.0001**
Normal	35	47.3	51	59.3	86	53.8	
Overweight	6	8.1	29	33.7	35	21.9	
Total	74	100	86	100	160	100	

Chi-square test; p<0.05 significant

Table 9. Correlation between BMI and PMI in Sarcopenic and Non-sarcopenic patients

BMI vs. PMI	Number	Correlation coefficient (r)	pvalue[P]
Sarcopenia group	74	0.319	0.98
Non-sarcopenia group	86	0.351	0.95

p - Pearson correlation test; p<0.05 significant

Table 8 presents the prevalence percentage of underweight, normal and overweight individuals in the sarcopenic and non-sarcopenic categories. It can be observed that about 47% of the CP patients in the ideal weight category were sarcopenic. Chi-square analysis indicated that BMI was associated with sarcopenia when compared to the non-sarcopenic group. To further evaluate if sarcopenia among the underweight CP patients correlated with PMI, a correlation analysis with Pearson's coefficient assay was carried out.

As indicated in Table 9, the study results did not reveal a correlation with BMI and PMI. Detailed studies have clearly demonstrated that there does not have to be a correlation between BMI and PMI. The majority of the sarcopenia patients diagnosed fall under the normal or ideal weight[9].

Table 10 presents PMI in diabetes, exocrine insufficiency, alcohol intake and smoking. Significant differences in the PMI scores between CP patients who had the complication and those who did not have the complication were observed. PMI was significantly different in diabetes and exocrine insufficiency.

The pathogenic progression of CP leads to complications such as malnutrition, exocrine insufficiency resulting in conditions such as Cirrhosis, Diabetes Mellitus, Sarcopenia. Since alcohol and smoking are strongly associated with the precipitation of CP and the progressive conditions, the present study looked into the prevalence of DM (Table 11), exocrine insufficiency (Table 12) and contributing factors such as smoking (Table 13) and alcohol intake in sarcopenia (Table 1).

Table 11 presents the percentage of sarcopenic and non-sarcopenic CP patients who had cirrhosis. While 16.2% of the patients in the sarcopenia group had cirrhosis, only 8.1% of the CP patients who did not present with sarcopenia had cirrhosis. Testing for the association of cirrhosis with CP did not reveal significance (p=0.115). Further large-scale studies in the south Indian population may reflect the actual association of cirrhosis in CP sarcopenia patients.

The manifestation of DM in the sarcopenia, non-sarcopenia CP group of patients was relatively higher, with 61% in the sarcopenic and 35% in the non-sarcopenic group (Table 11). In conjunction, Chi-square

Table 10. Comparison of PMI scores in various parameters

Variable	Yes			No			pvalue[T]
	Number	Mean	SD	Number	Mean	SD	
Diabetes	75	5.37	±1.69	85	6.1	±1.5	0.0053
Exocrine insufficiency	23	4.97	±1.4	137	5.89	±1.6	0.012
Alcohol	21	5.7	±1.54	139	5.75	±1.63	0.986
Smoker	25	5.58	±1.56	135	5.78	±1.6	0.572

*T-Two sample T test; Bolded p values are significant (p<0.05)

Table 11. Association between Sarcopenia and the presence of diabetes in the CP patients

Diabetes	Sarcopenia		Non-sarcopenia		Total		pvalue[C]
	Number	Percentage (%)	Number	Percentage (%)	Number	Percentage (%)	
Yes	45	60.8	30	34.8	75	46.9	0.001
No	29	39.2	56	65.1	85	53.1	
Total	74	100	86	100	160	100	

Chi-square test; p<0.05 significant; T2DM-60.8% Total -46.9%

Table 12. Association between sarcopenia and exocrine insufficiency in CP patients

Exocrine insufficiency	Sarcopenia		Non-sarcopenia		Total		pvalue[C]
	Number	Percentage (%)	Number	Percentage (%)	Number	Percentage (%)	
Yes	15	20.3	8	9.3	23	14.4	0.051
No	59	79.7	78	90.7	137	85.6	
Total	74	100	86	100	160	100	

Chi-square test; p<0.05 significant

Table 13. Association between sarcopenia and smoking status in CP patients

Smoker	Sarcopenia		Non-sarcopenia		Total		pvalue[C]
	Number	Percentage (%)	Number	Percentage (%)	Number	Percentage (%)	
Yes	13	17.6	12	13.9	25	15.6	0.530
No	61	82.4	74	86.1	135	84.4	
Total	74	100	86	100	160	100	

Chi-square test; p<0.05 significant; Smoking status: 17.6%, Total -15.6%

Table 14. Association between sarcopenia and alcohol in CP patients

Alcohol	Sarcopenia		Non-sarcopenia		Total		pvalue[C]
	Number	Percentage (%)	Number	Percentage (%)	Number	Percentage (%)	
Yes	11	14.9	10	11.6	21	13.1	0.545
No	63	85.1	76	88.4	139	86.9	
Total	74	100	86	100	160	100	

Chi-square test; p<0.05 significant; 14.9% sarcopenia, total 13.1%

analysis also revealed that the test for association of DM in sarcopenia was significant (p<0.001), indicating that a substantial population of the CP patients progressed to DM. On a similar note, exocrine insufficiency was nearly associated with sarcopenia in the present study (Table 12; p=0.051), indicating that the exocrine insufficiency participates in the pathogenesis of CP.

The study further assessed if smoking in the present study was strongly associated with sarcopenia, and it can be observed from Table 13 that about 18% of the smokers had sarcopenia, and 16% did not. The study results could not demonstrate an association in the chi square analysis (p=0.530), indicating that a larger sample size and baseline corrections could lead to a larger picture.

Table 14 in the present study indicates that among the sarcopenic CP patients, around 15% were alcoholics and that the prevalence of alcoholics in the CP patients without sarcopenia in the present study was attributed to around 12%. While it is well established that alcoholism is a major factor that is associated with CP in the western countries[6], in the

East/India, the prevalence of alcoholics in CP does not dominate[43]. A chi square analysis in the present study did not reveal a significant association of alcoholism in the CP population (p=0.545). Taken together, it can be understood that a significant percentage of CP patients with exocrine insufficiency and DM were sarcopenic.

Cumulatively, the present study results indicate that about 46% of the CP patient population was sarcopenic. PMI significantly differed between the male and female ($p<0.05$) CP patients, across the BMI categories ($p<0.001$), and between sarcopenic age 66-85 and nonsarcopenic age 66-85 category ($p<0.001$), between sarcopenic and nonsarcopenic underweight category ($p<0.001$). The study results also indicated that gender, age, BMI and DM are associated with sarcopenia. Both age, BMI did not correlate with PMI in the sarcopenia patients. Large-scale and elaborate studies are required to provide the best possible therapeutic interventions in advanced stages of CP.

6. Discussion

As an inflammatory disease and a syndrome with heterogeneity, CP causes morphological and functional distortion of the pancreas, and is primarily associated with exocrine insufficiency, malnutrition, sarcopenia and other severe complications. These complications are reported to increase infection risk, thrombolytic events and CP patients are also reported to have an increased risk of psychiatric illness, cancer of the pancreas[44]. Typically, a progressive reduction in skeletal muscle and strength that leads to disability and low quality of life is termed sarcopenia. Secondary sarcopenia in CP is associated with malnutrition, alcohol excess, limited physical mobilisation, cigarette smoking, and is differentiated from cachexia, frailty[11].

The common aetiology of CP is predominantly attributed to binge drinking, alcohol abuse in the western countries and the prevalence of CP in these countries has been estimated as 10-15 per 100000 people[6]. The prevalence of early CP in Japan has been reported to be 3.5 per 100000 in 2019[45]. Several studies across the globe have indicated that CP is more prevalent in men than women[6,46-48]. In India, CP is reported to be idiopathic, and there exists a paucity of information regarding CP prevalence. An early study from Kerala had reported that the prevalence in the community of IDDM (Insulin-dependent Diabetes Mellitus) was 125/100000 people[49]. Similarly, another early consensus report on the prevalence of CP in South India indicated that CP was prevalent in the range of about 114-120/100000 population in South India[22]. The study results also indicate that about 83% of the study population comprised males, and around 16% of the CP patient population were females. Similar to the results of these earlier studies, the present study, which was undertaken in Chennai, Tamil Nadu, indicated that the prevalence of CP in the community accounts to 1.6% per 10,000 people. Such studies have enabled the understanding that management of CP requires consistent follow-up and intervention at appropriate stages to prevent pathogenic progression and mortality.

Sarcopenia is defined and characterised by poor physical performance, poor muscle strength, and poor muscle quantity/quality. While ageing by itself is the primary cause for sarcopenia, secondary sarcopenia is a manifestation of an underlying disease process. Further, sarcopenia has been described as an independent predictor for worse surgical outcomes for complete pancreatectomy and islet auto transplantation[50]. Diagnosis of sarcopenia in CP using the psoas major muscle cross-sectional area is carried out at the L3 vertebral level using techniques such as CT, MRI, DXA, BIA and ultrasonography.

Computer-based Tomography (CT) of the psoas muscle has been used extensively in the diagnosis of sarcopenia, and the psoas muscle volume is negatively associated with ageing and body surface area[51,52]. Despite the common knowledge that sarcopenia can serve as an independent marker[12] in CP patients, only a few prevalence studies assessing sarcopenia in CP patients are available. Independent, earlier studies had indicated that approximately 33-52% of the CP patients were sarcopenic[13,50]. A 2020 review of literature study assessing the prevalence and impact of sarcopenia in CP patients reported 17-62%[34]. In conjunction with such studies, the present study results also indicate a high prevalence of sarcopenia among the CP patients, accounting for about 47%. Well-designed and detailed prevalence studies on CP patients indicate that the prevalence of CP among women was significantly less than males across the globe[5], and the present study also reflected such findings. Taken together, and of note, is that the aetiology of CP varies depending on tobacco

consumption, alcohol intake and given the regional differences in India, the present study has been the first initiative in Tamil Nadu to understand the prevalence of sarcopenia in CP patients. In the study, we also analysed the relevance of gender, age, BMI and other complications of CP in modulating PMI and associating with sarcopenia.

Analysis of the relevance of age, PMI among the sarcopenic and non-sarcopenic CP patients, revealed that PMI significantly varied in the sarcopenic patients belonging to the age group of 66-85, when compared to the non-sarcopenic group. However, the study results did not find an association between PMI and age. Supportive literature from earlier studies has also indicated that while malnutrition and pancreatic insufficiency are directly related to muscle index and decline in muscle mass, nutrition, in older sarcopenic patients, age has not been identified to be an independent entity in sarcopenic CP patients[4,8].

Since exocrine insufficiency, malnutrition and malabsorption are common in CP patients, trying to understand the distribution of body weight/BMI among the sarcopenic patients would provide a better insight into disease management. Therefore, the present study compared for significant variations in PMI across the BMI categories, and while we observed that the PMI between the underweight, normal and overweight categories varied significantly between the sarcopenic and non-sarcopenic groups, a significant correlation was not observed. Thus, the present study results, along with earlier studies, indicate that a correlation between BMI and PMI is not necessarily observed in CP patients. Adjunctive studies have also indicated that two-thirds of CP patients with low PMI had normal BMI, and about 22.5% in the assessed groups were obese, pinpointing that BMI could be a better index for nutritional assessments in the earlier stages of CP.

The present study further examined the prevalence of complications pertaining to CP and subsequently in the sarcopenic and non-sarcopenic groups. The results highlight that the PMI values among the CP patients in conditions like cirrhosis, DM, Exocrine Pancreatic Insufficiency (EPI) and with smoking, alcoholic aetiology significantly varied. Preceding studies have clearly demonstrated that EPI is strongly associated with sarcopenia, as it calls for adequate measures in addressing micro and macronutrient deficiencies, essential fats and fat-soluble vitamins, requires Pancreatic Enzyme Replacement Therapy (PERT). Other studies have also reported that EPI is co-incident in more than 50% of the patients with CP[53]. Ductal obstruction, alcoholism, atrophy and T2DM are also identified to increase the risk of occurrence of EPI to about 80%, and EPI incidence is reported to manifest 5-10 years after the onset of CP[54]. However, a huge lacuna in estimating the prevalence of CP and associated consequences, such as EPI, exists in the Indian scenario, and reference literature is limitedly available. As a first part of the report, the present study results reveal that about 14% of the CP patients and about 20% of the sarcopenic patients presented with EPI.

Progression of the chronic pancreatitis condition is typically characterised by fibrosis of the pancreas and results in exocrine and endocrine insufficiency. Consumption of alcohol activates the stellate cells and is associated with the induction of fibrosis in the pancreas and liver. Although the mechanisms between CP and liver cirrhosis are still being deciphered[55], cirrhosis is commonly reported in CP disease progression. As expected in sarcopenic patients[56,57] the present study data also pinpointed that the sarcopenia patients with cirrhosis were almost twice in number than the non-sarcopenic patients.

Similarly, cohort studies that were carried out to determine the influence of alcohol on CP have underscored that alcohol exacerbates the disease severity, and that alcoholic CP patients exhibited a 2-5 times accelerated progression to the late definite stage of CP[19,58]. A recent large retrospective study that analysed the influence of drinking pattern, abstinence from alcohol and nicotine in the disease progression reveals that the drinking pattern influences the course of the disease. The study also pinpointed that abstinence from alcohol reduced the course of the disease, reduced pseudocysts, led to less exocrine insufficiency, less abdominal pain and did not progress rapidly to a definite stage of CP. Nicotine restriction, on the other hand, did not affect disease severity, and the pseudocyst development was directly related to cumulative exposure levels. Thus, both drinking and smoking have been considered predominant factors that increase the need for surgical intervention[59], due to disease progression in these CP patients. On the other hand, earlier studies have also underlined that the incidence of alcoholic CP, exocrine insufficiency has been reported

to be significantly higher in men than in women[60]. In the Indian context, a retrospective study in CP patients has also revealed that idiopathic CP attributed to 75% of the aetiology, and alcohol attributed to the remaining 25%. Yet another longitudinal study that followed up the pathogenic progression of CP observed that the incidence of steatorrhea and diabetes was related to the onset age of CP. Further, the study details revealed that age onset, smoking history and alcoholic aetiology were significantly associated with pancreatic cancer incidence in the CP patients[61]. In conjunction with these earlier studies, the present study results have also indicated that about 14% of the sarcopenic CP patients were alcoholic, and reiterates the need to raise awareness, as alcohol is a major contributor to CP in the south Indian population[43]. However, such studies also underscore the need for conducting large cohort/longitudinal studies in the Indian CP patients.

While it is well known that smoking is a causative, precipitator for CP, detailed investigations of smoking in CP reveal that the smokers displayed significant differences in the CP age onset, type of pain and in the early development of diabetes mellitus when compared to alcoholic CP. The studies also bring to light that smokers developed steatorrhea earlier than other CP patients. However, they exhibited a delay in pancreatic stone formation. A 2022 systematic review and meta-analyses study that analysed the CP patient population from the east and west revealed that smoking related to CP was observed in 25.5% of the eastern population, while 42% of the western population of CP were smokers[62]. Another prospective study that compared CP aetiology across North America reveals that about 24% were past smokers and about 47% were current smokers[63]. However, the present study results reveal a relatively lower percentage of smokers (17%) among the sarcopenic CP patients.

One of the most frequent complications of CP is DM, and large-scale cohort studies that compare the western population and the eastern population have observed a mean prevalence of 30% in the east when compared to 33% in the west[22]. Similarly, a recent 7-year longitudinal study from China observed that the prevalence of diabetes is around 26.32% in CP patients. In a nation-wide prospective study carried out in 2008 in India, the incidence of DM in the CP patients was observed to be around 41%[64]. Trending closer, the present study identified that CP influenced DM was incident in 49%, and in 61% of the sarcopenic CP patients. Of note, research studies have also indicated that CP could be underdiagnosed, and a large-scale cohort study indicated that about 35% of T2DM patients were also diagnosed with pancreatic insufficiency. In conjunction with other prior studies[65,66], the present study data have also revealed that DM is significantly associated with sarcopenia in CP patients. Taken together, this prevalence study underscores the importance of regular interventional measures, follow up, for preventing/delaying the onset of sarcopenia in the CP patient population.

7. Summary and Conclusion

- The present study results reveal that sarcopenia is prevalent in 46% of the CP patient study population.
- Age, gender, and BMI categories had significant variations in PMI between the sarcopenic and non-sarcopenic groups, and male gender was significantly associated with sarcopenia.
- Complications like DM (47%), EPI (14.4%) in the sarcopenic CP patients had a higher prevalence when compared to non-sarcopenic CP patients, and DM was significantly associated with sarcopenia.

The study, as a first initiative, underscores the critical role of sarcopenia in CP disease progression and highlights the importance of early diagnosis with PMI and CT. The study underlines the need for targeted interventions, including nutritional and lifestyle modifications, to improve patient outcomes, thereby laying the foundation for future multicentric research that would address the complications of CP in diverse populations.

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