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ORIGINAL RESEARCH—CLINICAL

Geographic Differences in the Quality of Life Associated With Chronic Pancreatitis: An International, Multicenter Study

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BACKGROUND AND AIMS: Chronic pancreatitis (CP) is a disease that is present in multiple different geographic populations and is treated similarly around the world. No study has directly compared geographic differences in clinical characteristics of CP populations from Western and other regions, nor quality of life experiences. **METHODS:** This cross-sectional, multicenter study of adults (≥18 years) with definite CP recruited subjects at 4 centers from the Pancreatic Pain Consortium. Demographics, clinical and disease characteristics, and patient-reported outcomes, including Hospital Anxiety and Depression Scale and European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire Core 30 scores were obtained. Due to similarities in population characteristics, European and United States subjects were grouped together into a Western population. **RESULTS:** A total of 528 subjects were included (Indian n = 254, Western n = 274). Compared to the Indian cohort, the Western cohort had higher mean age at enrollment (54.5 ± 13.5 v 35.9 ± 11.8 years), older age distribution, higher rates of current alcohol use (34% v 2%) and alcohol etiology of CP (53% v 17%), more constant pain (50% v 20%), higher prevalence of exocrine pancreatic insufficiency (66% v 44%), and higher rates of endoscopic treatment (61% v 43%) (all $P < .001$). The Western cohort also reported lower global health and worse scores in physical, role, cognitive, and social functioning with a reduction in overall global health in multivariable regression analyses (−7.2 points [95% confidence interval −13.5 to −1.0] $P = .023$). **CONCLUSION:** There appear to be demographic, etiological, and quality of life differences in the experience of CP across different populations. Reasons for these differences, including potential cultural and societal forces, need to be further explored.

Keywords: chronic pancreatitis; geographic differences; life quality; quality of life

Introduction

Chronic pancreatitis (CP), a condition characterized by inflammation and fibrosis[1] of the pancreas, poses significant challenges in clinical management and profoundly affects patients' quality of life (QOL).[2] Multiple etiological risk factors contribute to CP, including genetic predisposition, environmental factors, and lifestyle choices such as alcohol consumption[3] and smoking.[3] These factors result in a complex clinical presentation and management challenges. There is substantial geographic variability in CP prevalence,[4] etiology,[5] and outcomes[6] seen across different geographic populations, highlighting the need for a comprehensive understanding of its impact on patients worldwide.

QOL is increasingly recognized as a key outcome in CP.[7] It is recognized that individuals with the same disease and severity, but from different environmental and cultural backgrounds, may perceive and value health outcomes differently.[8] This study aims to explore the demographic, clinical, and disease characteristics of CP patients across different geographic regions and their association with QOL. By examining aspects such as global health, physical and social functioning, and symptoms like pain and fatigue across dispersed geographical areas (India, the United States [USA], and Denmark), this research seeks to identify aspects of geographic differences in QOL among CP patients. Understanding these differences is crucial for developing targeted interventions and optimal management strategies to improve the lives of CP patients worldwide.

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Abbreviations used in this paper: **AP, Acute Pancreatitis; CI, Confidence Interval; CP, Chronic Pancreatitis; CT, Computed Tomography; DM, Diabetes Mellitus; EORTC QLQ-C30, European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire Core 30; EPI, Exocrine Pancreatic Insufficiency; HADS, Hospital Anxiety and Depression Scale; QOL, quality of life; SD, standard deviation.**

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Methods

Study Design

This was a cross-sectional multicenter study performed between October 2016 and November 2023 at four high-volume tertiary referral centers in the USA, Denmark, and India. The study cohort was comprised of adults (≥18 years of age) who had a diagnosis of CP as determined through review of the Cambridge criteria (either Cambridge III or IV or evidence of pancreatic calcifications on cross-sectional imaging such as computed tomography), or review of the multiple risk factor classification (M—multiple risk factor classification, A—alcohol consumption, N—nicotine consumption, N—nutritional factors, H—hereditary factors, E—efferent pancreatic duct factors, I—immunological factors, M—various rare miscellaneous and metabolic factors [M-ANNHEIM]).[9,10] Subjects were excluded if they had a history of abdominal pain from other causes (ie inflammatory bowel disease, gastroparesis, etc.) with symptoms that were unable to be distinguished from CP pain, if they were known to be pregnant, had a history of pancreatic malignancy or other active malignancy, or were unable to provide informed consent.

Demographic and Clinical Characteristics

Data on demographics and clinical and CP disease characteristics were obtained via case report forms completed by subjects at enrollment. Alcohol etiology of CP, prior history of acute pancreatitis, pancreatic endotherapy (including endoscopic retrograde cholangiopancreatography, extracorporeal shockwave lithotripsy, or pancreatic surgery were noted. Age at the onset of CP was recorded. Tobacco use was reported as past, present, or never. Current alcohol consumption was categorized into abstainers (no alcohol use or <20 drinks in a lifetime), light-to-moderate drinkers (light: <3 drinks/week, moderate: 4–14 drinks/week for males, 4–7 drinks/week for females), heavy drinkers (15–34 drinks/week for males, 8–34 drinks/week for females); and very heavy: >35 drinks/week for both genders).[3] Pain pattern at the time of enrollment was characterized generally as constant, intermittent (including prior pain episodes that had resolved), or never.[11] A previously existing diagnosis of exocrine pancreatic insufficiency (EPI)[12] or diabetes mellitus at enrollment was also recorded.[13]

Health-Related QOL Assessment

The multilingually validated European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30) questionnaire was used to assess QOL in all populations.[14] The EORTC questionnaire is multidimensional and allows for a thorough understanding of the impact of CP on various aspects of daily life; it has additionally been validated in CP patients.[14,15] The EORTC QLQ-C30 consists of three sections, each with a score that ranges from 0-100. It has one global domain named global health; one functional domain with five items (physical functioning, role functioning, emotional functioning, cognitive functioning, and social functioning); and a symptom domain with nine items (fatigue, nausea and vomiting, pain, dyspnea, insomnia, appetite loss, constipation, diarrhea, and financial difficulties).

We also looked for symptoms of anxiety and depression using the Hospital Anxiety and Depression Scale (HADS).[15] The HADS is a self-rating questionnaire that is comprised of 14 items, in which respondents rate their experiences on a four-point Likert scale, ranging from "most of the time" to "not at all". It yields two subscores for depression and anxiety, respectively. Subscale scores range from 0 to 21, with 0-7 (normal), 8-10 (borderline), and 11 or higher representing the presence of anxiety or depressive symptoms. A cutoff score of >7 is applied to define abnormality, as utilized in previous studies and in the current studies.[16] The HADS has demonstrated good internal consistency, reliability, and validity in previous assessments,[17] supporting its utility as a tool for evaluating anxiety and depression, and has previously been utilized in CP patients.[18]

Questionnaires were administered to subjects in English in the USA and India (verbal clarifications obtained in Hindi by the coordinator as needed) and Danish in Denmark.

Statistical Analysis

Continuous data were expressed as mean with standard deviation or median with interquartile range as appropriate, while categorical data were expressed as numbers (percentage). Comparisons were made between a Western cohort of subjects (created by combining those from the USA and Denmark due to similarities in those populations in mean age, age distribution, duration of disease, and racial characteristics)[18,19] and the Indian population. Direct comparisons of demographic, clinical, and Patient-Reported Outcome Measure–derived variables were conducted using Fisher's exact tests or Student's t-tests. In addition, multivariable regression analyses were performed to assess differences in QOL parameters between Western and Indian populations, with results presented as mean differences and 95% confidence intervals (CIs). The findings were reported across three models: Model 1, unadjusted; Model 2, adjusted for age and gender; and Model 3, adjusted for sex, age, current alcohol consumption, smoking, pain pattern, anxiety, depression, diabetes, EPI, previous endoscopy, and previous surgery. A P value of <0.05 was considered statistically significant. All statistical analyses were conducted using Stata (version 17; College Station, TX).

Results

Patient Demographics

A total of 528 subjects with CP were enrolled in the study: 274 from Western populations and 254 from the Indian population. Of the Western cohort, 58 subjects were from Denmark and 216 were from the USA (98 enrolled at the University of Pittsburgh and 118 at Johns Hopkins University). Table A1 contains the separate results by individual center. In reviewing the two groups, compared to the Indian cohort, the Western cohort was older (mean age 54.5 ± 13.5 vs 35.9 ± 11.8 years), more likely to have an alcohol etiology of disease (144 [53%] vs 44 [17%]), be current users of alcohol (93 [34%] vs 4 [2%]), tobacco (118 [43%] vs 33 [13%]), and have painful CP (240 [87%] vs 171 [67%]) (all $P < .001$). Rates of EPI (180 [66%] vs 111 [44%]) and previous endoscopic treatment (161 [61%] vs 105 [43%]) were higher in the Western cohort than in the Indian cohort (both $P < .001$). No significant differences were seen between the groups in duration of disease, opioid use, prevalence of anxiety or depression symptoms, diabetes, or rates of previous pancreatic surgery (see Table 1).

Table 1. Demographic and Clinical Characteristics of the Study Cohorts

	Total population (n = 528)	Western population (n = 274)	Indian population (n = 254)	*P* value
Male sex, n (%)	339 (64)	170 (62)	169 (67)	.318
Mean age, y ± SD	45.6 ± 15.7	54.5 ± 13.5	35.9 ± 11.8	<.001
Age distribution, n (%)				
<30 y	92 (17)	12 (4)	80 (32)	<.001
30–39 y	115 (22)	34 (12)	81 (32)	
40–49 y	102 (19)	43 (16)	59 (23)	
50–59 y	95 (18)	70 (26)	25 (10)	
60–69 y	85 (16)	78 (28)	7 (3)	
>70 y	39 (7)	37 (14)	2 (1)	
Current alcohol consumption, n (%)				
Abstainer	431 (82)	181 (66)	250 (98)	<.001
Light-to-moderate use	75 (14)	71 (26)	4 (2)	
Heavy-or-very-heavy use	22 (4)	22 (8)	0 (0)	
Alcoholic etiology, n (%)	188 (36)	144 (53)	44 (17)	<.001
Smoking, n (%)[a]				
Never smoker	293 (56)	76 (28)	217 (86)	<.001
Past smoker	82 (16)	80 (29)	2 (1)	
Current smoker	151 (29)	118 (43)	33 (13)	
Median duration of CP diagnosis, y (IQR)[b]	5 (2-9)	5 (2-9)	5 (1-9)	.314
Pain pattern, n (%)				
No pain	119 (23)	34 (12)	85 (33)	<.001
Intermittent pain	221 (42)	102 (37)	119 (47)	
Constant pain	188 (36)	138 (50)	52 (20)	
Opioid use, n (%)[c]	269 (51)	130 (48)	139 (55)	.117
HADS, n (%)[d]				
Anxiety	227 (45)	125 (48)	102 (42)	.178
Depression	185 (37)	92 (36)	93 (38)	.578
Diabetes mellitus, n (%)	224 (42)	108 (39)	116 (46)	.159
Exocrine pancreatic insufficiency, n (%)[e]	291 (55)	180 (66)	111 (44)	<.001
Previous endoscopic treatment, n (%)[f]	271 (52)	166 (61)	105 (43)	<.001
Previous pancreatic surgery, n (%)[g]	59 (11)	30 (11)	29 (12)	.890

CP; chronic pancreatitis, HADS; Hospital Anxiety and Depression Scale; IQR, interquartile range; SD, standard deviation.
[a]Information on smoking was missing for two patients.
[b]Information on the duration of CP, was missing for 13 patients.
[c]Information on opioids was missing for two patients.
[d]HADS, questionnaire was missing for 28 patients; HADS, anxiety or depression score >7 was taken as indication of anxiety and depression, respectively.
[e]Information on exocrine pancreatic function was missing for three patients.
[f]Information on previous endoscopic therapy was missing for seven patients.
[g]Information on surgery was missing for seven patients.

Quality of Life

In univariable analysis, the Western cohort reported a significantly lower overall global health score on the EORTC QLQ-C30 compared to the Indian population (Table 2). Worse scores for physical, role, cognitive, and social functioning were also seen in the Western cohort compared to their Indian counterparts (Figure 1), with the difference in perceived role functioning being the most pronounced (all $P < .001$). The emotional functioning domain was the only area where no significant differences were seen between the two groups ($P = .158$). The Western cohort scored slightly higher in this domain than their Indian counterparts. Worse scores for fatigue, nausea and vomiting, pain, dyspnea, insomnia, appetite loss, and diarrhea were also seen in the Western cohort compared to the Indian cohort (all $P < .001$). Scores for symptoms of constipation ($P < .001$) and financial difficulties ($P = .004$) were worse in the Indian cohort than in the Western cohort (Table 2).

In multivariable analysis (unadjusted, Model 1), significantly worse functional scores for the domains of physical (mean difference −11.6 points [95% CI −15.1 to −8.0], $P < .001$), role (mean difference −22.3 points [95% CI −27.7 to −17.0], $P < .001$), cognitive (mean difference −10.3 point [95% CI −14.6 to −5.9], $P < .001$), and social (mean difference −12.6 points [95% CI −17.8 to −7.4], $P < .001$) functioning were reported by the Western cohort compared to the Indian cohort (Table 3). When adjusted for age and sex (Model 2), significantly worse functional scores were still reported by the Western cohort compared to their Indian counterparts in the same domains. When the model was

Table 2. EORTC QLQ-C30 Subscales and Items in the Western and Indian Chronic Pancreatitis Populations

	Western population (n = 274)	Indian population (n = 254)	Mean difference (95% CI)	*P* value
Global health	52.7 ± 25.8	61.8 ± 25.0	−9.1 (−13.5 to −4.8)	<.001
Functional scales				
Physical functioning	73.5 ± 22.1	85.1 ± 19.0	−11.6 (−15.1 to −8.0)	<.001
Role functioning	59.3 ± 33.7	81.6 ± 27.6	−22.3 (−27.7 to −17.0)	<.001
Emotional functioning	65.2 ± 26.8	61.9 ± 27.4	3.3 (−1.3 to 8.0)	.158
Cognitive functioning	70.3 ± 27.8	80.6 ± 22.3	−10.3 (−14.6 to −5.9)	<.001
Social functioning	64.1 ± 32.9	76.7 ± 27.1	−12.6 (−17.8 to −7.4)	<.001
Symptom scales/items				
Fatigue	49.3 ± 27.5	34.6 ± 29.3	14.7 (9.8 to 19.5)	<.001
Nausea and vomiting	26.5 ± 30.1	14.6 ± 26.0	11.9 (7.1 to 16.7)	<.001
Pain	52.7 ± 34.3	25.5 ± 30.9	27.2 (21.6 to 32.7)	<.001
Dyspnea	18.0 ± 26.9	8.8 ± 21.1	9.2 (5.1 to 13.4)	<.001
Insomnia	47.7 ± 37.6	29.7 ± 37.8	18.0 (11.6 to 24.5)	<.001
Appetite loss	38.2 ± 35.9	25.2 ± 34.7	13.0 (7.0 to 19.0)	<.001
Constipation	20.3 ± 29.5	31.8 ± 37.8	−11.4 (−17.2 to −5.7)	<.001
Diarrhea	27.3 ± 31.7	4.3 ± 16.3	22.9 (18.6 to 27.3)	<.001
Financial difficulties	35.4 ± 37.4	45.1 ± 39.7	−9.7 (16.3 to −3.1)	.004

further adjusted (Model 3), the difference in physical functioning was only borderline significant (mean difference −4.9 [95% CI −9.9 to 0], $P = .053$). Significantly worse scores in the same pattern (worse in Western compared to Indian population) were seen in role (mean difference −16.8 points [95% CI −24.2 to −9.4], $P < .001$), cognitive (mean difference −6.1 points [95% CI −12.2 to 0], $P = .049$), and social functioning (mean difference −14.3 points [95% CI −21.8 to −6.8], $P < .001$) (Table 3). No differences in emotional functioning were seen in any of the models.

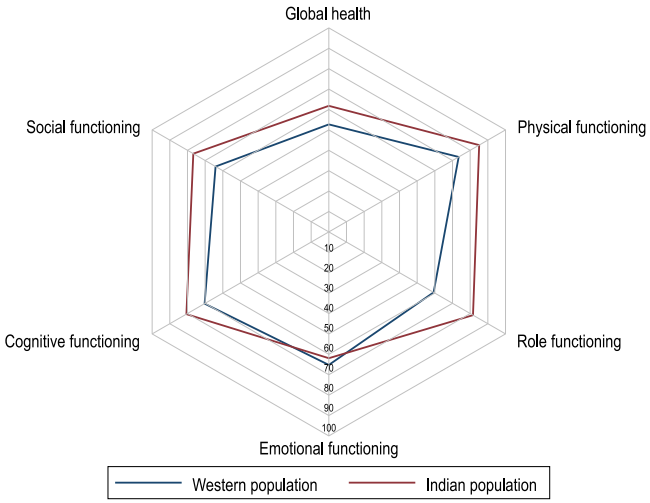

Figure 1. Comparison of EORTC-QLQ C30 global health and functioning scores between patients in the Western cohort (blue) and Indian cohort (red). Those in the Western cohort reported significantly lower global health, physical functioning, role functioning, cognitive functioning, and social functioning than those in the Indian cohort. The Western cohort reported slightly higher emotional functioning scores than did the Indian cohort, though this did not reach statistical significance.

Discussion

To our knowledge, this is the first study to directly compare QOL in patients with CP across distinct geographic cohorts. The study reveals that Western patients have different characteristics including a younger age, higher prevalence of alcohol etiology, higher rates of endotherapy, and report significantly worse QOL and functioning scores compared to their Indian counterparts. Notably, the difference in perceived role functioning between cohorts was substantial, with Western patients experiencing a significantly lower ability to fulfill work-related and personal role expectations. In contrast, the Indian cohort reported greater financial difficulties and constipation symptoms, indicating different stressors affecting their QOL. These findings highlight the complex interplay of socioeconomic factors and health-care practices influencing patient experiences and outcomes in CP.

Structural and Cultural Differences

Western countries have high rates of health insurance coverage (80%–85%) that can help to lower out-of-pocket costs for patients who might otherwise experience financial hardship in the setting of chronic disease.[20] In India, there is increasing prevalence of both private and government insurance coverage, however the rates of utilization of these services is unknown, and high out-of-pocket expenses to purchase medical care may result in hardship or delaying necessary care.[20,21] This may be further exacerbated by patient's choice of treating center, whether private or government-sponsored. Data are lacking in how differences in pain beliefs and perceptions between Western and Indian CP patients may impact pain management and patient outcomes.[22] However, it should be acknowledged that differences in social and cultural attitudes have a crucial impact

Table 3. Multivariable Analyses of EORTC QLQ-C30 Global Health and Functional Scales by Chronic Pancreatitis Population (Western Population vs Indian Population)

	Model 1		Model 2		Model 3	
	Mean difference (95% CI)	*P* value	Mean difference (95% CI)	*P* value	Mean difference (95% CI)	*P* value
Global health	−9.1 (−13.5 to −4.8)	<.001	−11.1 (−16.5 to −5.6)	<.001	−7.2 (−13.5 to −1.0)	.023
Functional scales						
Physical functioning	−11.6 (−15.1 to −8.0)	<.001	−7.9 (−12.2 to −3.5)	<.001	−4.9 (−9.9 to 0)	.053
Role functioning	−22.3 (−27.7 to −17.0)	<.001	−23.8 (−30.4 to −17.2)	<.001	−16.8 (−24.2 to −9.4)	<.001
Emotional functioning	3.3 (−1.3 to 8.0)	.158	0.5 (−5.2 to 6.3)	.857	0.8 (−5.1 to 6.7)	.788
Cognitive functioning	−10.3 (−14.6 to −5.9)	<.001	−9.4 (−14.8 to −4.0)	.001	−6.1 (−12.2 to 0)	.049
Social functioning	−12.6 (−17.8 to −7.4)	<.001	−16.4 (−22.8 to −9.9)	<.001	−14.3 (−21.8 to −6.8)	<.001

Model 1: Unadjusted (crude).
Model 2: Sex and age adjusted.
Model 3: Adjusted for sex, age, current alcohol consumption, smoking, pain pattern, anxiety, depression, diabetes, EPI, previous endoscopy and previous surgery.

on the experience of patients suffering from a painful chronic disease.

Abdominal Pain and QOL

Previous studies have shown that constant pain in CP is associated with lower QOL,[23] with factors like psychiatric comorbidities,[18] alcohol etiology[24] and sleep disturbance[25] only partially explaining the impact on QOL.[24] In this study, the prevalence of constant pain was higher in the Western population (50%) compared to the Indian population (20%). Prior research has shown lower QOL in patients with constant pain compared to intermittent or no pain, which may partially explain the results we see here.[26] CP pain is also known to affect mental health, and previously, the presence of psychiatric comorbidity has been associated with lower QOL compared to CP in the absence of psychiatric comorbidity.[18] Interestingly, we found no significant differences in anxiety and depression between the Western and Indian populations despite the majority of the Western population having lower QOL and higher constant pain prevalence.

Functionality and QOL

Functionality scores in this study remained significantly lower for the Western cohort even after adjusting for confounding factors, suggesting an inherent disparity in the impact of CP in the two groups. This was further evidenced by the higher scores reported for symptoms traditionally associated with a lower QOL, such as fatigue, nausea, and pain, underscoring the burden of CP on daily living. Despite a lower score in physical functioning on univariate analysis, the multivariable analysis suggested only a borderline significance when adjusted for comprehensive demographic and clinical factors, which may indicate the multifaceted etiology of functional impairment in CP.

Alcohol, Smoking, Opioid Use, and QOL

Differences in age, smoking, alcohol, EPI, and frequency of previous endoscopic therapy were seen between Western and Indian populations. While factors such as younger age, female sex, smoking, alcohol consumption, diabetes, and EPI have been associated with lower QOL in CP, their association has been inconsistent across studies.[27–29] A large US cohort notably showed that physician-defined alcohol etiology and prior endoscopic or surgical treatments did not independently affect QOL.[30] Inconsistencies between studies in these factors may be due to variability in the instruments used to determine QOL, regional differences in the care of CP patients, relative sample size of studies, and heterogeneity of studied cohorts.

The Indian cohort reported a much lower smoking prevalence than the Western cohort in this study. The effect of smoking on QOL in CP has been inconsistently reported, but some studies have suggested that smoking may be associated with poorer QOL.[2,28,31] Smoking may contribute to CP disease progression through the formation of calcifications, more pronounced fibrosis, or worsening of exocrine and or endocrine function. However, any mechanisms by which smoking affects QOL remain unclear and should be further studied.

In this study, no significant differences were seen in rates of opioid use between the Indian and Western cohorts. Opioids are known to be widely prescribed for chronic pain management in the USA,[32] with a complex impact on QOL in CP patients. Previous studies have shown that depression, QOL, and alcohol use were associated with opioid misuse in CP patients.[33] While opioids can provide significant pain relief and improve QOL for some patients,[34] they also pose risks of side effects, dependency, and mental health issues without necessarily providing optimal pain relief.[35] Less is known about opioid prescribing practices for CP in India, though recent studies suggest that many Indian patients receive low-potency opioids on an as-needed basis for pain.[36] The prevalence of opioid use in this study suggests

that there is more to learn about the type and duration of opioid use for CP patients in all areas of the world, including the effect that these medications have on QOL.

Significance of Geographic Differences in QOL

The significance of QOL findings between countries and regions may be important to take into account as multicenter studies are planned for testing of CP treatments. QOL is an essential outcome measurement in CP. This study represents the first direct comparison to our knowledge of QOL in Western and Indian CP cohorts, providing an important understanding of how these populations compare at baseline. As many studies are now conducted across multiple continents, it may be important to consider adjusting for the geographic origin of the cohort when analyzing multinational studies.

Limitations

Although this study has multiple important strengths including the large cohort of CP subjects, the careful phenotyping of disease, and adjustment for multiple confounding factors in multivariable analyses, several limitations should be acknowledged. Recruitment and study procedures were performed at tertiary centers, which may introduce selection bias and limit the generalizability of the findings to the overall CP population. While only a single center from India was included, this is a tertiary care center with a referral population from a very large catchment area and comparable to the combination of referral patterns seen in Western centers. We note that inclusion from a single Indian center may also create limitations.[37] Although multivariable analysis was used to control for differences in study populations, inherent differences between Western and Indian patients, such as varying etiologies of CP, may still affect the results (ie, residual confounding). Grouping the Danish and American patients together may have obscured subtle differences between these populations. In addition, we were unable to account for important demographic factors such as income, family size, ethnicity, marital status, availability and access to health insurance, employment, and education level, which could further influence the QOL and health-care access. Nutritional status and dietary preferences were also unable to be accounted for. These limitations highlight the need for further research with more diverse and representative samples to validate and expand upon our findings.

Conclusion

In conclusion, our study delineates a stark contrast in QOL outcomes for CP patients from Western and Indian cohorts, rooted in a matrix of demographic, clinical, and potentially cultural factors. The implications for clinical practice are profound, advocating for a personalized approach to CP management that accommodates the nuanced needs of different populations. Future research should aim to unravel these complex interactions further, supporting the evolution of targeted interventions that could enhance QOL for CP patients globally.

Supplementary Materials

Material associated with this article can be found, in the online version, at https://doi.org/10.1016/j.gastha.2025.100720.

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