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SYSTEMATIC REVIEW AND META-ANALYSES

Epidemiology and Characteristics of Chronic Pancreatitis—Do the East and West Meet?

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BACKGROUND AND AIMS: Previous large studies on the epidemiology and clinical profile of chronic pancreatitis have suggested significant differences in presentation and management in the eastern and western hemispheres. The aim of this systematic review was to compare large multicenter studies across different geographic regions of the world to detect meaningful differences in the presentation and management of this poorly understood disease. **METHODS:** We identified 237 manuscripts through a comprehensive literature review aiming to identify multicenter studies enrolling more than 200 patients to limit reporting biases. After rigorous screening, 12 studies were included for the final analysis. The Asian studies were included in the eastern cohort, and the European and American studies were included in the western cohort. Reported demographics, risk factors, etiologies, clinical presentation, complications, and management strategies were then compared. **RESULTS:** We found similar demographics across both cohorts including age, prevalence among gender, and predominant etiology. Clinical manifestations including pain, pancreatic calcifications, and diabetes were similar between both cohorts although pseudocysts, pancreatic cancer, and strictures were more common in the west. Notably opioids and surgical/endotherapy management were more common in the west as well. **CONCLUSION:** Chronic pancreatitis is a protracted disease affecting predominantly middle-aged people, leading to a decreased quality of life. Chronic pancreatitis now appears to have a fairly similar clinical profile and natural history in the east and west. There is notable variability in management. We hope that international collaboration may identify common targets for research which could lead to significant advances in the understanding and management of chronic pancreatitis.

Keywords: Chronic Pancreatitis; East; West; Global Epidemiology

Introduction

The last few decades have seen rapid advances in understanding of disease pathophysiology and new treatment paradigms which were inconceivable during the latter half of the 20th century. These advances include identification of chronic diseases and neoplasia progression pathways along with previously unknown checkpoints for which targeted immunotherapy or genetic therapy is being developed, often with great success.

These advances have also been greatly beneficial for several chronic gastrointestinal diseases ranging from chronic diarrhea to aggressive inflammatory bowel diseases where certain molecular therapies and immunotherapies have greatly improved the quality of life and prognosis for patients.[1]

Chronic pancreatitis (CP) remains one of the enigmatic diseases where unfortunately, so far, we have remained spectators to a smoldering disease progression. There are a myriad of presentations and poor outcomes that have a significant impact on both the patient's quality of life and also more broadly on society due to sizeable health-care costs and loss of productivity.[2]

This disease is widely prevalent across the globe; however, significant differences exist in presentation and management across various countries. These differences could be due to a variety of factors which may include difference in etiologies, host factors, clinical presentation, and access to health care but also could very well be due to various biases that may exist in regional studies including selection, recruitment, or lead time biases. The purpose of this systematic review is to report on the epidemiology, presentation, and management of CP across various regions in the world and to analyze if there indeed is a difference in etiologies, clinical profile, and/or natural history of this disease across regions. We hope that comparing the disease broadly

Abbreviations used in this paper: **BMI, body mass index; CP, chronic pancreatitis; MRI, magnetic resonance imaging; TCP, tropical calcified pancreatitis.**

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Table 1. Studies Included in the Primary Analysis

Ref no.	Authors, year of publication, country	Design	Number of patients included
3	Ryu JK, Lee JK, Kim YT et al. Digestion. 2005;72(4):207–11. South Korea	Retrospective multicenter cohort	814
4	Lévy P, Barthet M, Mollard BR et al. Gastroenterol Clin Biol. 2006 Jun-Jul;30(6–7):838–44. France	Nationwide survey to physicians	1748
5	Balakrishnan V, Unnikrishnan AG, Thomas V et al. JOP. 2008 Sep 2;9(5):593–600. India	Prospective multicenter cohort	1033
6	Wang LW, Li ZS, Li SD et al. Pancreas. 2009 Apr;38(3):248–54. China	Retrospective multicenter cohort	2008
7	Frulloni L, Gabbrielli A, Pezzilli R et al. Dig Liver Dis. 2009 Apr;41(4):311–7. Italy	Prospective multicenter cohort	893
8	Bang UC, Benfield T, Hyldstrup L et al. Gastroenterology. 2014 Apr;146(4):989–94.	Retrospective multicenter cohort	11,972
9	Hirota M, Shimosegawa T, Masamune A et al. Pancreatology. 2014 Nov-Dec;14(6):490–6. Japan	Nationwide survey to physicians	1734
10	Ali UA, Issa Y, Goor H et al. Pancreatology. 2015 Jan-Feb;15(1):46–52. Netherlands	Prospectively administered questionnaires to patients	1218
11	Domínguez Muñoz JE, Lucendo Villarín AJ, Carballo Álvarez LF et al. Rev Esp Enferm Dig. 2014 Jul;108(7):411–6. Spain	Nationwide survey to physicians	Not reported
12	Szücs Á, Marjai T, Szentesi A et al. PLoS One. 2017 Feb 16;12(2):e0171420. Hungary	Prospective multicenter cohort	229
13	Conwell DL, Banks PA, Sandhu BS et al. Dig Dis Sci. 2017 Aug;62(8):2133–2140. USA	Prospectively administered questionnaires to patients and physicians	521
14	Bellin MD, Whitcomb DC, Abberbock J et al. Am J Gastroenterol. 2017 Sep;112(9):1457–1465. USA[a]	Prospectively administered questionnaires to patients and physicians	1171
15	Olesen SS, Poulsen JL, Drewes AM et al. Scand J Gastroenterol. 2017 Aug;52(8):909–915. Scandinavia/Baltic	Prospective multicenter cohort	910

[a]Data from Conwell and Bellin studies combined for analysis.

across the east and the west will improve understanding of this disease and guide future collaborative research to identify specific disease-modifying etiologic factors and management strategies which could alleviate some of the long-term suffering with chronic pancreatitis.

Methods

A literature search using major databases such as PubMed, Embase, and Ovid was performed by investigators using the following search words: (CP OR CP[Mesh] OR CP[tw] OR CP [tiab] OR Pancreatitis, Chronic* AND/complications OR Pancreatitis, Chronic* AND/diagnosis OR Pancreatitis, Chronic* AND/therapy OR Pancreatitis, Alcoholic/epidemiology OR Pancreatitis, Chronic/complications OR Pancreatitis, Chronic/etiology*) AND (Geographic Locations OR Africa OR Americas OR Antarctic Regions OR Arctic Regions OR Asia OR Europe OR Oceania OR Population Groups OR Demography/statistics AND numerical data OR Geographic Locations[tw] OR Africa[tw] OR Americas[tw] OR Antarctic Regions[tw] OR Arctic Regions[tw] OR Asia[tw] OR Europe[tw] OR Oceania[tw] OR Population Groups[tw] OR Geographic Locations[Mesh] OR Africa[Mesh] OR Americas[Mesh] OR Antarctic Regions[Mesh] OR Arctic Regions[Mesh] OR Asia[Mesh] OR Europe[Mesh] OR Oceania [Mesh]) AND (Registry OR prospectively OR Prospective Studies OR Registries OR Risk Factors).

Prior published guidelines and comprehensive review articles were also reviewed to identify relevant references.

Only English language studies were included. To limit referral or other biases, single-center studies and those with less than 200 patients were excluded. Since several of the studies were registry-based studies, only the latest publications from these registries at the time of literature review were included, and smaller studies utilizing the same databases were also excluded. Studies were published over a 12-year period ranging from 2005 to 2017. Cognizant effort was made to select the single most inclusive study from individual countries or regions with 2 independent reviewers screening for eligibility based on inclusion criteria. Reviewers and subsequent analysis attempted to ascertain risk of bias, imprecision, inconsistency, and publication bias with selected studies measured per Grading of Recommendations, Assessment, Development and Evaluations criteria as having moderate to high certainty of evidence. Studies evaluating patients <18 years of age were also excluded from this review. Using the described search strategy, 237 records were initially identified, and abstracts reviewed for eligibility. Of these, 44 full-text articles were screened for eligibility, and 12 studies were selected for primary analysis (Table 1, Figure 1). We then completed the

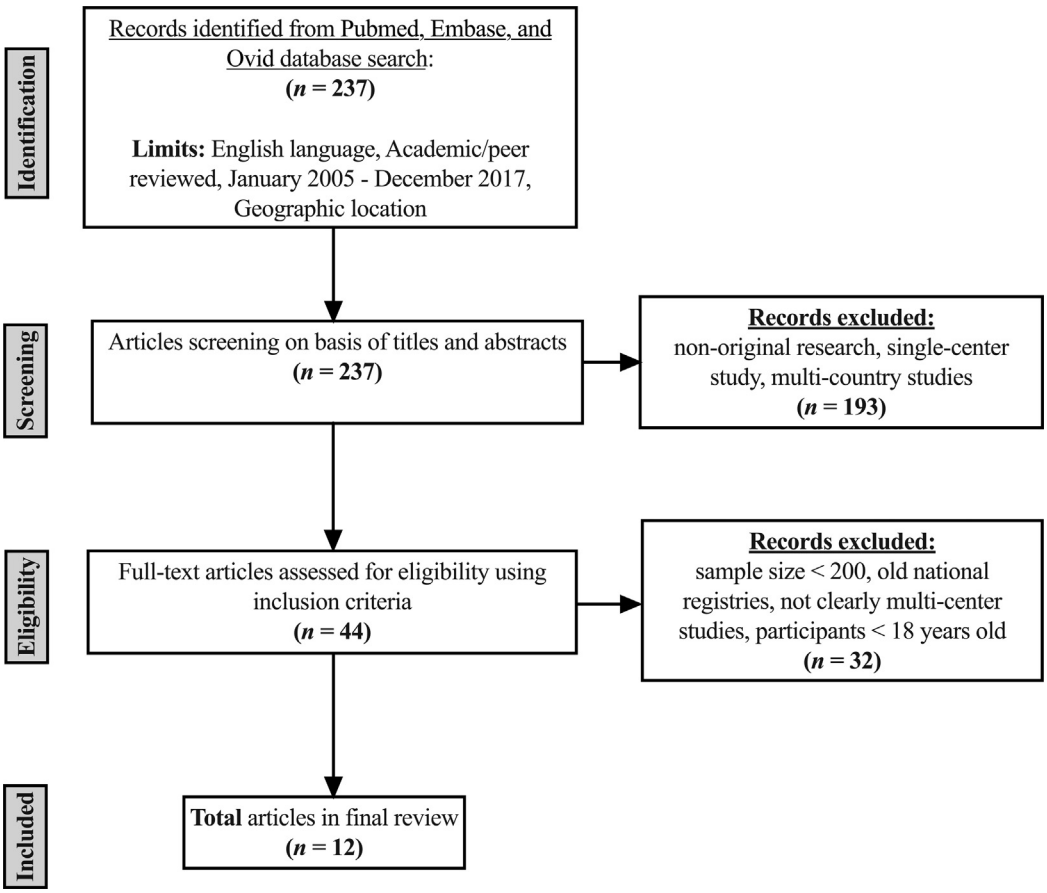

Figure 1. Article identification, inclusion, and selection flowchart.

Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 checklist for our systematic review.[16]

The available data were analyzed under the following subheadings:

i. Epidemiology which included mean or median age, mean disease duration, gender distribution, body mass index (BMI), and etiology. Due to differences in classification within the reviewed literature, the etiology was categorized as alcoholic or nonalcoholic. The nonalcoholic category was then further queried to categorize the disease into the following groups where available: biliary stone disease, idiopathic, pancreas trauma, hereditary/genetic pancreatitis, autoimmune, obstruction, others. Tropical pancreatitis as an etiology was only reported in 1 study from India and was therefore not analyzed separately.

ii. Clinical presentation included presenting complaints (categorized as pain, jaundice, weight loss, steatorrhea, diarrhea, or clinical malabsorption); presence of calcifications; and complications categorized as pseudocysts, biliary strictures, pancreatic neoplasm, diabetes mellitus, fistula or ascites, gastrointestinal bleeding, vascular complications including pseudoaneurysms or splenic vein thrombosis, and portal hypertension.

iii. Finally, we also reviewed and compared the management strategies including the use of surgery, endotherapy, and opioids across these various cohorts (Table 2).

Table 2. Demographics

	East (n = 5589)	West (n = 5519)
Gender (%)		
Male	4169 (74.6)	3998 (72.4)
Female	1420 (25.4)	1521 (27.6)
Etiology (%)		
Alcohol	2799 (50.1)	3353 (60.8)
Nonalcohol	2790 (49.9)	2166 (39.2)
Non-alcoholic etiology (%)		
Idiopathic	775 (13.9)	494 (9.0)
Smoking	1423 (25.5)	2319 (42.0)
Other	3781 (67.7)	3578 (64.8)
Complications (%)		
Pain	4138 (74.0)	2220 (40.2)
Calcifications	2278 (40.8)	2747 (49.8)
Biliary strictures	467 (8.4)	529 (9.6)
Pseudocysts	2934 (52.5)	1439 (26.1)
Diabetes mellitus	1683 (30.1)	1816 (32.9)
Management (%)		
Endotherapy	490 (8.8)	1306 (23.7)
Surgery	416 (7.4)	844 (15.3)

Four studies from India, China, Japan, and South Korea were included in the eastern cohort, and the rest of the studies from Europe and the United States were included in the western cohort.

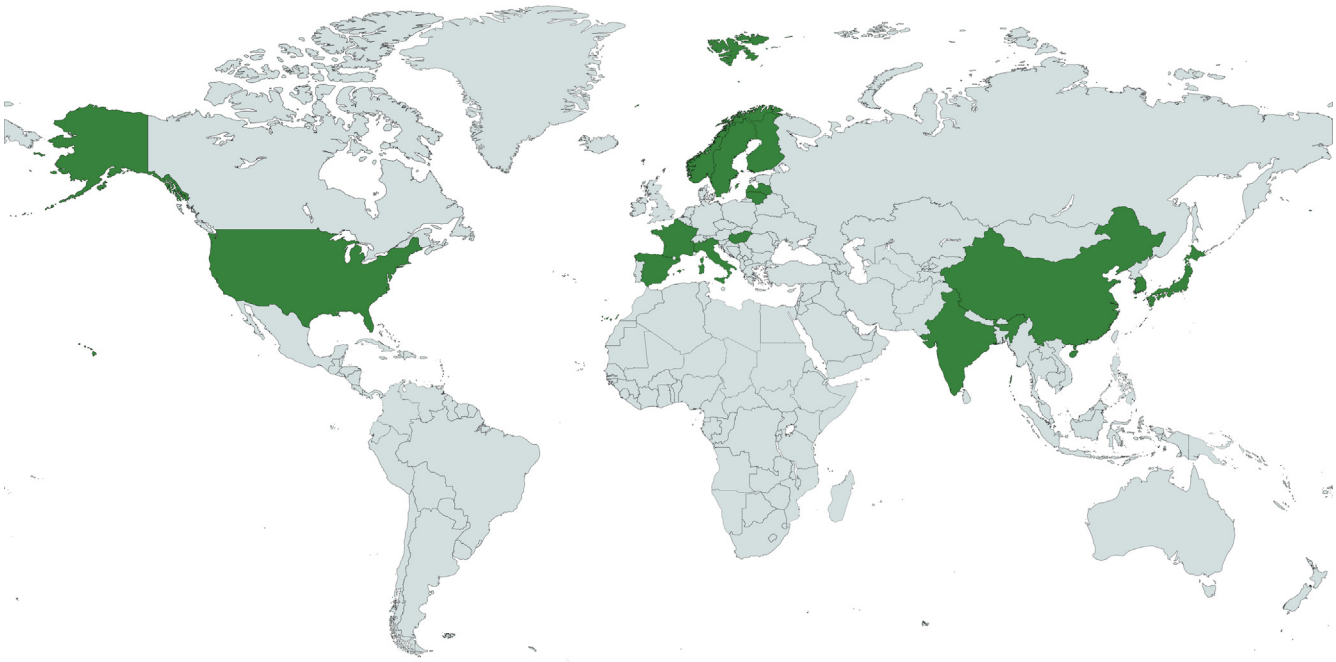

Figure 2. Global distribution of selected studies.

All the abovementioned data points were not available in each of the selected studies; therefore, various parameters were assessed as available.

Furthermore, in discussing our findings, we looked at qualitative measures to determine similarity in epidemiology, presentation, and management of the east and west cohorts. All percentages were converted into proportions, and statistical analysis was performed using proportions and the total sample in the studies. We computed the effect size of the proportions for all the studies that had complete data. Heterogeneity among studies was computed as Q and I^2. For all computations, an alpha level of 0.05 was used. In the present study, we computed both the fixed and random effects. However, we used random effect and mixed model for the interpretation of results. The statistical analyses and computations were done using Comprehensive Meta-Analysis version 3.3.070 (Biostat, Englewood, NJ).

Results

Of the 12 multicenter studies included in the review, 4 were from Asia (India, China, Japan, and South Korea),[3,5,6,9] 1 from the United States,[13] and 7 from Europe.[4,7,8,10,12,15,17] The global distribution of these studies is presented in Figure 2. Three studies used retrospective cohorts for their data, 9 utilized prospectively maintained databases, and 3 were based on surveys to a wide sample of physicians. One of the included studies also included prospective patient survey questionnaires.[13] The sample size of these studies ranged from 229 to 11,972.[1,2] The study by Bang et al[8] which included 11,972 participants was an outlier as it was a nationwide registry study from Demark and included all patients from 1995 to 2010.

Epidemiology

The age distribution is presented in Figure A1A and ranged from 40 to 62 years. Although the study from India reported the youngest mean age of patients, on comparing the eastern to the western cohort, overall there was no significant difference in age between the east and the west. The Japanese survey which had the oldest mean age (62 years) was also notable for the longest disease duration of 10 years at the time of inclusion.[9] The duration of disease where reported ranged from 3.5 years (France) to 9.7 years (Japan).[4,9] Women were less likely to have CP than men and constituted between 14%[3] and 45% of all patients[13] across different studies with no significant differences between the east and the west cohort (23% vs 30%) (Figure A1B). The mean or median BMI was normal for 3 (India, Italy, and Scandinavia) of the 4 studies where it was reported. In the American cohort, half of the patients had a BMI >24.[13]

There was a wide range of patients who were presumed to have alcohol as the primary etiology, ranging from 35% (China[6]) to 84% (France[4]) (Figure A1C). However, on comparing the eastern cohort to the western cohorts, these differences became much less prominent with a mean of 51.5% (34.1%–68.5%) in the east to a mean of 58.2% (48.3%–67.4%) in the west (Figure A1C). The nonalcoholic etiologies were not well described across different studies. Three Asian studies (China, South Korea, and Japan)[3,6,9] reported idiopathic pancreatitis ranging from 12.9% (China) to 20.8% (South Korea) which was very similar to the range reported in the western studies 8%–24%.[4,7,13,15] Across all studies, idiopathic etiologies were more commonly reported in women than in men. Five studies (China, Japan, Italy, USA, and Scandinavia) reported on

hereditary or genetic causes as etiologies. Four of these 5 studies listed 4%–10% of these patients as having genetic causes as an etiology.[6,7,13,15] The Japanese study was an outlier with only 0.6% patients identified as having genetic or hereditary causes for their CP.[9] Similarly, Wang et al[6] listed biliary stone disease as an etiology in 34.3% of patients in their cohort from China. This is unique as biliary stone disease has not been reported as a major etiology in any other cohort.[6]

Clinical Presentation

Pain was the most frequent clinical manifestation across all the studies and ranged from 52.7% at the lower end in the French cohort[4] to 91% in the Indian cohort.[5] In all other cohorts, pain was reported in between 60% and 80% of patients (Figure A2A). On comparing the east and the west, pain was reported more frequently in the Asian cohort (Figure A2B). Three European studies further categorized pain into constant vs intermittent pain with different results. The Scandinavian Baltic database reported continuous pain in only 18% of patients with 44% of patients having intermittent or recurrent pain. The Spanish cohort reported similar results with 49% of patients having recurrent or intermittent pain vs chronic pain in 30.6% of patients. On the other hand, in the Italian data set, 71% of patients had continuous pain.[7,11,15] The second most prevalent symptom was clinical malabsorption which was reported in 5 of the 12 studies. Wang et al[6] reported malabsorption in 36% of their population from China, and studies from France, Hungary, Spain, and the United States reported a similar prevalence of malabsorption ranging from 35% to 39%.[4,11,12,14] Other symptoms that were reported at least 1 time in an eastern or western study included jaundice (13.4% China; 9% Italy), weight loss (10.4% China; 11.5% Hungary; 28% Italy), and steatorrhea (7% China; 13% Hungary; 21% in Italy and Spain).

Pancreatic calcifications, which were one of the defining characteristics of CP in all the studies, were reported in 4 studies and appeared to be similarly distributed among eastern and western studies (64.9%, confidence interval 58.4%–70.1%) (Figure A2C).

Tobacco as a risk factor for CP was evaluated in 7 of the 12 studies (2 eastern, 5 western). Even though tobacco use was not quantified in all 7 studies, in the eastern cohort, ever smokers were most common in the Japanese cohort at 75% and least common in the Indian cohort at 28%, possibly referring to only current smokers.[5,9] The western cohort reported a prevalence of ever smokers ranging from 53% (Netherlands) to 70% in the Scandinavian-Baltic Database.[10,15]

Diabetes was the most frequent complication reported in 10 of the 12 studies. Prevalence of diabetes appears to be similar in the eastern and western cohorts, with a mean prevalence of 30.1% (21%–40%) in the east and 32.9% (10%–37%) in the west (Figure A2D).

Pancreatic pseudocysts and biliary strictures were the most commonly reported local complications. Prevalence of pseudocysts was less commonly documented in the eastern cohort and ranged from 16% (India) to 28% (South Korea).[3,5] Comparatively in the western cohort, it ranged from 23% (USA) to 40% (France)[4,14] (Figure A2E). The prevalence of biliary strictures was similar where reported and ranged from 8% to 14% in the eastern cohort and 9% to 16% in the western cohort (Figure A2F). Levy et al[4] reported a 21.3% prevalence of extrinsic compression of the bile duct, but it was not clear if this compression could be considered a true biliary stricture due to CP. Other inconsistently reported complications included ascites (1.7% China; 2.3% India; 6.6% South Korea), gastrointestinal bleeding (0.4% China; 1.6% India), and pseudoaneurysm (0.3% India; 1.4% Spain). Pancreatic malignancy was another observed local complication of CP that led to high mortality, with 4 of 12 studies commenting on its prevalence. Technically, the prevalence of pancreatic cancer was higher in the western cohort at 10.2% in the Netherlands but was only quantified in 1 western study.[10] Multiple eastern studies looked at the prevalence of pancreatic cancer with overall lower rates of 3.1% and 4.7% in South Korea and India, respectively, while China had a higher rate at 7.9%[3,5,6] (Figure A2G).

Management Strategies

Reporting on specific management strategies was not the objective in the included studies; however, most of them broadly reported on the percentage of patients who underwent surgery or endotherapy in their respective cohorts. Intervention with surgical management was lower in the eastern cohort with a range of 8%–12% vs a wider range in the western cohort 8%–31%[3,5–7,10,13–15] (Figure A3A). The details of surgical procedures were not provided in most studies but included both resection and drainage procedures.

Similar to surgical intervention, patients in the western cohort were significantly more likely to undergo endotherapy at 41.4% (36.5%–46.4%) than those in the eastern cohort at 13.8% (6.7%–26.5%)[5–7,10,12–15] (Figure A3B). Endoscopic procedures included pancreatic and biliary sphincterotomies, pancreatic and biliary stent placements with or without lithotripsy, and cyst drainage procedures.

Data were sparser for pancreatic enzyme replacement therapy and noninvasive pain management. Wang et al[6] reported in their study from China that all patients in their cohort were given pancreatic enzyme supplements; however, other Asian studies did not report on pancreatic enzyme supplement use. In the western cohort, pancreatic enzyme supplement use was reported in 5 studies and ranged from 41% to 65%.[7,11,12,14,15] Opioid analgesic use for pain relief was 31% in the South Korean cohort[3] and ranged from 21.7% to 35% in the 3 western studies that reported on opioid use.[11,14,15] In addition, another 32.5%

intermittently used opioid analgesics in the North American Pancreatitis Study 2 cohort from the USA.[14]

Discussion

In the present review, we evaluated and compared the clinical profile of CP across various regions of the world. We ultimately found a fairly consistent global pattern. Broadly, CP is most prevalent in the middle-aged population (40–62 years) and more frequently reported in men (55%–85%). Notably, it appears to affect much younger patients in India possibly due to genetic predisposition.[18] Although alcohol remains the most common etiology, the more recent studies suggest that alcohol may be an etiology in only a third to half of the patients. Globally, the clinical phenotype appears remarkably similar. Most patients have calcifications, and pain is the most frequent manifestation of CP (60%–80%).

Undoubtedly, different cohorts had certain unique features or characteristics which diverged from the global picture, but as we discuss them, it is important to recognize that these studies had vastly different study designs as reported in Table 1. Some of the discrepancies could be due to inherent biases associated with retrospective or observation studies such as classification, selection, reporting, or recall bias among others.

The criteria for defining chronic pancreatitis varied across the studies. While most older studies relied on ductal changes and calcifications to make the diagnosis, the more recent European studies utilized classification systems like M-ANNHEIM, while the Japanese study utilized the Japanese society criteria.[3–5,9,12,15] The USA study also utilized imaging characteristics to diagnose chronic pancreatitis but differed from the eastern studies in that more patients underwent magnetic resonance imaging (MRI) and/or endoscopic ultrasound (EUS).[13] EUS and MRI are more sensitive for diagnosing noncalcified chronic pancreatitis, and the use of EUS or MRI in more recent studies may explain some of the difference in calcification rates that we report.[19] Interestingly, pain, pattern, or severity has not been shown to be associated with calcifications and is reflected in this review as well.[20] Traditionally, it has been suggested that most patients in the west have alcoholic chronic pancreatitis while most patients in the less-developed nations have other etiologies for chronic pancreatitis.[21,22] We did find the older western studies (France 2006, 83.6%), compared to studies from South Korea (2005, 64%) and Japan (2014, 68%), which are considered industrialized nations rather than developing, did report a higher prevalence of alcoholic pancreatitis.[5,9,16] However, the more recent western studies (USA, Italy, Hungary) report less than 50% of patients to have alcoholic pancreatitis.[7,12,13] It is not clear why this paradox exists. It could certainly suggest that alcohol abuse is declining in the west, but there is no concrete evidence to suggest this decline.[23] Our interpretation is that previous studies have overclassified patients as alcoholic pancreatitis, and with advances in classification systems and recognition of other etiologies, this overestimation is being corrected. Furthermore, the median age for alcoholic pancreatitis was very similar across various studies suggesting that racial and ethnic differences in alcohol metabolism may not significantly influence the pathogenesis of alcoholic pancreatitis.[24]

Among the etiologies for nonalcoholic pancreatitis, Wang et al[6] report that 34% of their cohort had a biliary etiology for chronic pancreatitis. The association between gallstones and chronic pancreatitis is unique to China because gallstone disease has not been associated with chronic pancreatitis in other cohorts. However, several studies from China have reported this association, and the suggested hypothesis is that an obstructive etiology results in chronic pancreatitis from recurrent acute pancreatitis due to delay in definitive treatment for gallstone disease.[25] Recent large studies from China however do not suggest that gallstone disease is a common etiology for chronic pancreatitis.[26] Other nonalcoholic etiologies like genetic or autoimmune were not well studied across various cohorts but globally accounted for 5%–10% of all patients with chronic pancreatitis. Finally, on review of the articles, there is limited information regarding long-term prognosis of CP based on etiology. In the South Korean population, it was found incidence of diabetes ($P < .05$) and pseudocysts ($P < .05$) were higher in patients with alcoholic CP vs in those with nonalcoholic etiologies.[3] Determining whether etiology of CP predicts a specific long-term prognosis would be interesting to further examine as it may help predict the trajectory of disease a patient faces on diagnosis.

Notable outliers for mean age of patients were the study from India[5] where the mean age was 40 years and the study from Japan[9] where the mean age was 62 years. The older age of the Japanese cohort can be explained by a much longer disease duration (around 10 years) prior to inclusion in the study. The younger age in the Indian study appears to be consistent with other larger single-center studies done in different regions of India where the mean age ranged from 36 to 40 years.[27,28] Traditionally, the younger age of onset in South Asia has been attributed to tropical calcified pancreatitis (TCP)[29]; however, in the included Indian study, only 3.8% of patients were diagnosed with TCP. This is similar to other recent Indian studies where the mean age of the cohort has been less than 40 years even though TCP has been attributed as an etiology in less than 6% of the patients.[18,28] Recent studies from India have shown that the phenotype of CP has changed over time and suggested the term "TCP" as a misnomer.[18] The younger age at presentation in the Indian cohort has been attributed to early-onset idiopathic chronic pancreatitis which may be associated with certain mutations like *SPINK1* or *CFTR* gene polymorphisms.[18] One western study (Conwell et al[13]; USA) specifically evaluated early and late idiopathic chronic pancreatitis. In contrast to the Indian study, in the United States study, 69% of patients had late-onset idiopathic pancreatitis (defined as occurring after 35 years of age).[13] Broadly, genetic and autoimmune etiologies appear similar

across different regions; however, details of the mutations were not provided in most studies.

Overall, the majority of studies shared systemic and local complications, with some key differences between cohorts. Malabsorption and diabetes afflicted about a third of the patients, and this was similar in the east and west. In addition, biliary stricture occurred in about a fourth of the patients in both cohorts. On the other hand, pseudocysts and pancreatic cancer appear more common in the western cohort. Therefore, the natural history of chronic pancreatitis is fairly similar across the world, but there remain differences in local complications that should be further examined.

Despite the similar clinical profile of chronic pancreatitis across different countries, we found significant differences in the management of these patients. From these studies, it appears that patients in the western cohort were more likely to be on opioid medications and also more likely to undergo endoscopic or surgical therapy. While this may be due to better access to health-care resources in the more developed countries, it could also suggest that the nonopioid medical management options for chronic pain such as antioxidant therapy and dietary modification, which are more prevalent in the east than in the west, may contribute to pain relief and should accordingly be increasingly adapted in the west.[30,31]

One significant omission in our study is that we do not compare the incidence or prevalence rates of chronic pancreatitis across various regions. However, this omission is intentional because we believe that both the incidence and prevalence reporting are flawed in most studies on chronic pancreatitis. This is because although the life expectancy for chronic pancreatitis is between 20 and 35 years after diagnosis, where reported, the prevalence is just between 3 and 8 times the incidence rate.[4,9,17] This disparity may be due to attrition of patients following up over such a prolonged course of disease leading to underreporting of prevalence.

In addition to the difference in study designs that we have mentioned before, the studies included in our review were published over a 12-year period ranging from 2005 to 2017. There have been significant advances in our knowledge regarding etiologies, risk factors, and management of chronic pancreatitis, and these may influence some of our results. Finally, the review process for selection of the most representative article for each country and/or region was somewhat subjective based on the independent reviewers. However, we attempted to minimize this limitation with strict inclusion and exclusion criteria and 2 reviewers for screening and selection. Overall, despite these limitations, we feel this study has unique strengths. It compares studies from several different regions of the world resulting in a more accurate global representation of the clinical profile of chronic pancreatitis. Furthermore, we have included only large multicenter studies, thereby avoiding some of the inherent referral biases that may be present in single tertiary-center studies to hopefully provide a more real-world representation.

We conclude that CP is a protracted disease affecting predominantly middle-aged people, leading to a decreased quality of life and a significant economic and social impact on the community. Collating these data demonstrates that although divergent in the past, chronic pancreatitis has a fairly similar clinical profile in the east and the west. Globally there is increasing recognition that alcohol attributes to only about half of this chronic debilitating disease, and a significant proportion of patients do not yet have an identifiable etiology and are classified as idiopathic. Moreover, the natural history of this disease appears to be similar across the globe. Despite similarities in presentation, there are significant regional differences in management of these patients. These findings are definitively hypothesis-generating. For example, are the differences in etiologies only responsible for the initial trigger following which the pathogenesis of this disease becomes fairly similar? How can we reliably quantify and treat pain in the majority of patients who are not candidates for endoscopic or surgical therapy? Why do people in the east require less opioids than the west? Are patients offered opioids more in the west? Are there disease-modifying targets we can identify that may help in altering the natural history of CP? Clearly there are many more unanswered questions regarding this enigmatic disease. We hope that international collaboration may help answer some of these questions by identifying common targets for research which could lead to significant results.

Supplementary Materials

Material associated with this article can be found in the online version at https://doi.org/10.1016/j.gastha.2022.07.013.

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The corresponding author, on behalf of all authors, jointly and severally, certifies that their institution has approved the protocol for any investigation involving humans or animals and that all experimentation was conducted in conformity with ethical and humane principles of research.

Data Transparency Statement:
The authors will provide supplementary figures summarizing data related to various complications of chronic pancreatitis.