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ORIGINAL RESEARCH

Direct costs for nonsurgical management of Chronic Pancreatitis in a tertiary care teaching hospital

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ABSTRACT

Background: Chronic pancreatitis (CP) is a leading cause of hospitalization among gastrointestinal diseases resulting in considerable financial burden to patients. However the direct costs for nonsurgical management in CP remains unexplored.

Methods: A cross sectional study was carried out (2011–14) in the Department of Gastroenterology, Kasturba Hospital, Manipal, India. Demographic and clinical data on laboratory investigations, interventions and follow up were obtained from the medical records department. Item costs were derived from the hospital electronic billing section. Cost was expressed as median annual cost per patient.

Results: 65 (male 48; 73.8%) patients were included. Their median age was 31 (range 12–68) years. The annual median (IQR) total cost per patient was INR 88,892 (70,550.5–116,004); [USD 1410(1119–1841); € 1155(916–1507)], comprising of INR 61,089 (39,102.5–90,360.5) [USD 970 (621–1434); € 793(508–1174)] for outpatient management and INR 32,450 (11,016–46,958) [USD 515 (175–745); €421(143–610)] for hospitalization. 69.5% of the treatment cost was attributed to outpatient treatment. Drugs contributed to 54%, hospitalization incurred 30.5%, investigations 12% and professional fees (3.5%) of the total cost. Pancreatic enzyme replacement therapy (PERT) cost contributed to three-quarters of drug therapy. Use of rabeprazole as against pantoprazole reduced the overall annual cost of therapy by 4%.

Conclusions: This study depicts the first nonsurgical management of accrued direct costs associated with CP due to expensive medications. Due to the high cost for PERT, its usefulness needs proper validation by cost benefit analysis.

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KEYWORDS
Chronic pancreatitis; pharmacoeconomics; direct cost; pancreatic enzyme replacement therapy; cost of illness

1. Introduction

Chronic pancreatitis (CP) is a progressive illness marked by recurrent or persistent inflammation leading to permanent damage to the pancreas [1,2]. The age at diagnosis is 32–58 years [3]. The incidence of CP is 4.35/100,000 [4] and prevalence in western countries is 42/100,000 [5] while in southern India it is 126/100,000 [6]. Progressive disease can result in calcification and atrophy of the organ, leading to recurrent or persistent abdominal pain, weight loss, steatorrhea, and glucose intolerance [7,8]. Causes of CP include excessive alcohol consumption, smoking, pancreas divisum, hyperparathyroidism, cystic fibrosis, or it could be idiopathic in nature [9–11]. Patients with CP need hospitalization to treat painful flares and complications such as pseudocysts and pancreatic ascites [12,13]. In spite of lower incidence and prevalence, it affects patients' quality of life substantially due to unendurable abdominal pain [14] and can result in pancreatic cancer in a small proportion of patients over time.

The cost of illness (COI) of a disease identifies its burden to the society expressed in monetary terms [15,16]. CP is a major cost driver as these patients need long-term follow up. Yet, there is hardly any study around the world to assess the costs associated with the nonsurgical management of CP patients.

2. Methods

This study was carried out in a 2032 bedded Kasturba Medical College hospital situated in Manipal, Karnataka over a 3-year period (2011–2014). Patients were identified retrospectively from the medical records department and billing databases for CP as the primary diagnosis. ICD-9-CM 577.1 (For CP the medical code changed to ICD-10-CM K86.1 from 2015 October) along with specialty were used to search patients with CP. The billing database was searched by patient's name and hospital number to see the details and number of procedures performed, hospitalization charges, and the amount paid. Patient information was also retrieved from hospital discharge summaries. Details obtained from patient case files included variables like age, gender, duration of follow up, investigations, length of hospital stay, and medical treatment. Patients who underwent surgical therapy for CP were not included.

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Supplemental data for this article can be accessed here.

2.1. Patient evaluation

Patients had been evaluated for etiology, presence of complications, and diabetes mellitus (DM). CP was diagnosed on the basis of standard guidelines [12] and featuring any 2 of typical upper abdominal pain, elevation of serum amylase and lipase above three times the upper limit of normal and changes of pancreatitis on abdominal imaging [ductal changes/calcifications and one or more of abdominal ultrasound, computed tomography, endoscopic ultrasonography EUS (consistent with and 'suggestive of' CP by the Rosemont criteria) or magnetic resonance cholangiopancreatography] [11,17]. The management of CP in our department included initial evaluation with complete blood count, serum calcium, triglycerides, blood glucose, liver function test, stool analysis, pancreatic enzymes amylase and lipase. Paracentesis (diagnostic or therapeutic) was done in those with pancreatic ascites or pleural effusion. Fluid analysis included white cell count, differential count, culture and sensitivity, amylase, lipase, adenosine deaminase, lactate dehydrogenase, total proteins and albumin. Fasting and postprandial plasma glucose, HbA1c (% of glycated hemoglobin) had been used to diagnose DM and to optimize the dose of antidiabetic medications.

2.2. Management

Patients admitted with severe abdominal pain were initially managed with intravenous fluids, intravenous analgesics, and nil per oral regimen. Oral feeds were initiated with clear liquids when the pain had subsided and switched to solid food as tolerated at the earliest. Long-term management included oral pancreatic enzyme replacement therapy (with meals or snacks), antioxidants and a proton pump inhibitor (PPI) prior to breakfast [18,19]. Patients not responding to drug therapy underwent endotherapy. Patients not responding to endoscopic therapy were referred for surgery [12,20]. Patients who had impaired glucose levels had been advised diabetic diet. Metformin was used most often and glimepiride/glipizide and insulin were added as necessary to ongoing treatment. De-addiction therapy including acamprosate was used for alcohol dependence. Vitamin D and B_{12}, calcium, iron, and folic acid supplements were prescribed when appropriate. The other most commonly prescribed drugs were amitriptyline or dothiepin for depression and domperidon for vomiting. Patients were asked to come for routine health checkup at every 1–3 months depending on their clinical condition.

2.3. Direct estimates of outpatient, inpatient costs and statistical analysis

For every patient, direct cost (per annum) was obtained by multiplying units utilized by unit cost. The Kasturba hospital, Manipal price list was used as the reference for unit costs. Values are expressed in Indian rupee (INR). Costing included a micro costing, prevalence-based, retrospective approach over 1 year period [21]. The statistical analysis was done by SPSS® software package (v.21). Descriptive statistics (frequency, percentage, SD, median, interquartile range) were used to analyze the costs. To convert costs to US dollars ($) and Euros (€), the market exchange rate for the month of December 2014 was used which was INR 63 and INR 77 converted and rounded it to the nearest $ and €, respectively [22]. The cost analysis included the expenses related to the physician's consultation fees, investigations, for prescribed medicines. For inpatient cost, charges for hospitalization, nursing, charges for general/special ward per diem and cross consultation to other departments, if any were included additionally. Cost analysis included initial diagnostic investigations as well the management cost after establishing the diagnosis. Direct costs for endoscopic retrograde cholangiopancreatography (ERCP) included drugs and IV equipment, contrast agent, and physician fees. The charges for material used such as papillotomes, guidewires, gloves, oxygen tubings, laundry, etc.) have been included (Supplementary table).

3. Results

Of the 67 patients with CP evaluated for the study over a 3-year study period, 2 (3%) were lost to follow up after a single visit. Data from 65 patients (male = 48 (73.8%)) were analyzed. The cause was alcohol in 14 (21.5%) and cigarette smoking in 18 (27.7%) of patients. Their baseline characteristics are shown in Table 1. 24 (36.9%) responded to drug therapy, 41(63.1%) underwent endoscopic therapy. Most of the CP patients (~98%) had to get admitted more than once over a 1-year period, abdominal pain being the commonest reason. 64 patients had 185 hospitalizations contributing to an average of 2.9 hospitalizations per patient over a one year period.

The estimated cost for CP per hospitalization ranged from INR 2455 (USD 39; €32) to INR 58,564 (USD 929; € 761). The annual median (IQR) total cost per patient was found to be INR 88,892 (70,550.5–116,004) (Figure 1); [USD 1410(1119–1841); € 1155(916–1507)], for outpatient management was INR 61,089 (39,102.5–90,360.5) [USD 970 (621–1434); € 793 (508–1174)], for hospitalization was found to be INR 32,450 (11,016–46,958) [USD 515 (175–745); €421(143–610)] (Table 2). Drug cost incurred 54%, hospitalization incurred 30.5%, investigations 12%, and professional fees (3.5%) of the total cost. The annual mean per patient cost for PERT was INR 29,565 (USD 469; €384) and INR 5475 (USD 87; €71) for antioxidants (Figure 2). The annual mean cost of using rabeprazole was INR 1679 (USD 26; €22), esomeprazole INR 1825 (USD 29; €24), pantoprazole INR 2555 (USD 41; €33). Smoking cessation with bupropion incurred mean cost of INR 1674 (USD 27; €22) for 3 months while de-addiction with acamprosate incurred INR 8250 (USD 131; €107) for 5 months. 5 (7.7%) patients had been noncompliant to drugs for affordability issues over a 1-year period. Two patients had stopped drugs for 20 days and 1 month, respectively. However, in the other three patients, the exact time duration for which the drugs were stopped was not evident. Alcoholic patients incurred 1.3 times higher cost than nonalcoholic due to increased cost for procedures and de-addiction. Patients on insulin had to spend 28% more than those on oral

Table 1. Demographics and clinical characteristics of patients.

Variable	CP n (%)
Male	48 (73.8)
Female	17 (26.2)
M:F	2.8:1
Median age yrs (range)	31 (12–68)
Abdominal pain	65 (100)
Vomiting	23 (35.4)
Number of pain episodes per year median(IQR)	3 (2–4.5)
Disease duration in months median(IQR)	24 (4.5–48)
Alcoholic pancreatitis	14 (21.5)
Cigarette smokers	15 (23.1)
Alcohol + Cigarette smokers	3 (4.6%)
Idiopathic pancreatitis	33 (50.8)
Diabetes mellitus	22 (33.8)
Hypertension	3 (4.6)
Hypertriglyceridemia	2 (3)
Epilepsy	1 (1.5)
Retroviral Illness	1 (1.5)
Calcification	45 (69)
Pseudocyst	11 (16.9)
Pancreatic ascites	7 (10.8)
Metropolitan status	
Rural	42 (64.6)
Urban	23 (35.4)
Average no of drugs prescribed per visit	2 (1.75–3)
Number of procedures mean±SD	2.5 ± 1.5
Annual OP visits median (IQR)	8 (5.5–13.5)
Emergency room visits	35 (53.8)
No of days of hospitalization median (IQR)	8 (2.25–12)
Died during hospitalization	2 (3.07)
USG median	2 (1–4)
OP Consultations	8 (5.5–13.5)
IP Consultations	2 (1.5–4)
X-ray abdomen	65 (100)
Ultrasound Abdomen	65 (100)
ECG	45 (69.23)
Computed Tomography	38 (58.46)
MRCP	5 (7.7)
ERCP	41 (63.1)
EUS	21 (32.3)
UGI	39 (60)
Referral to other departments	
Psychiatry	14 (21.5)
Clinical psychology	4 (6.1)
Dermatology	5 (7.7)
Hospital room category utilized	
General	47 (72.3)
Semi Private	8 (12.3)
Private	10 (15.4)

Table 2. Direct cost involved in treating chronic pancreatitis patients.

Components of Cost	Amount in INR(Rs.) Median(IQR)
Registration at hospital	400 (280–460)
Annual doctor consultation fees	533.33 (366.67–900)
Investigations	826 (540–3048)
Antidiabetic	2993 (670.75–22,625)
PPI	2783 (2093–4677.5)
Analgesic	950 (650–1750)
Others	694 (335–1220)
Median cost per patient at first visit	4438 (1126–7591)
With PERT	52,395.66 (33,784.83–79,059.66)
Without PERT	17,465.22 (11,261.61–26,353.22)
Alcohol	
Yes	101,620 (84,023–130,125)
No	90,916 (79,265–105,263)
Smoking	
Yes	137,377 (98,642–146,529)
No	84,257 (78,162–102,864)
Diabetes	
Yes	53,563 (34,874.5–81,809.5)
No	51,193 (32,564.5–79,346)
Outpatient Cost	61,089 (39,102.5–90,360.5)
Hospitalization Cost (Inpatient)	32,450 (11,016–46,958)
Total Cost	88,892 (70,550.5–116,004)
% of Cost distribution	
Consultation	3.5%
Investigations	12%
Hospitalization	30.5%
Drugs	54%
Direct Costs	100%
Outpatient Cost	69.5%
Hospitalization Cost	30.5%

hypoglycemic agents. The cost in those with pancreatic pseudocysts was 1.8 times that of those without ($p < 0.001$). On an average, patients with DM spent 1.3 times as much as those without this sequelae. Two patients had died due to pancreatic cancer.

All patients needing ERCP were hospitalized. The average hospital stay for ERCP was estimated to be 4 days. 41 (63.1%) had ERCP procedures during their one year of follow up. All were done for therapeutic purposes. Pseudocysts were successfully drained under EUS guidance in all cases 11 (16.9%) slated for the procedure with no major complications. Patients who underwent EUS and ERCP had a mean annual costs of INR 70,282 (USD 1116; €913) and INR 100,233 (USD 1591; €1302), respectively. Medical interventions incurred additional costs for antibiotics, though antibiotics and tests amount to <12% of the total cost. The unit cost of ERCP, pancreatic duct stone removal, pancreatic sphincterotomy with ductal stenting and pseudocyst drainage costs are shown in Supplementary table.

4. Discussion

By retrospectively analyzing the medical records of CP patients in a tertiary care center over a 3-year period, we assessed the annual total direct COI in these patients. Our study showed that the costs for CP is mainly driven by drugs and hospitalization. Drugs accounted to 54% of the total direct cost. Of this, 72% was accounted for PERT in our study. PERT and antioxidants have been shown to reduce pain in CP [23,24]. No studies have looked for QOL or long-term outcomes with PERT. However, a recent meta-analysis suggests that the role of PERT for the management of pain, steatorrhoea, and weight loss in CP remains equivocal [25].

Adherence rate comes down due to more frequent dosing of drugs [26,27]. Patients often skip a dose to prolong the time to a medication refill due to the high cost of medicines. 5 (7.7%) patients in the study were noncompliant to drugs due to affordability issues. For CP, PERT and antioxidants need to be taken thrice a day. The pancreatic enzyme brands available in India vary in terms of content for amylase, lipase, and protease and the cost varies from INR 18,068 (USD 287; €235) to INR 95,922 (USD 1523; €1246) per year. The formulations also differ by enteric/nonenteric coating and composition. For the treatment of pain of CP, the enzyme preparations preferably need to be non-enteric coated. While lipase is important for steatorrhea, proteases are vital for pain reduction. Prolonged use of pancreatic enzymes can lead to hyperuricemia and fibrosing colonopathy; hence, adverse reactions need to be kept in mind. There is no doubt that PERT is expensive but weighing the expected costs raises the question of the quantum of benefit these drugs will provide in CP. More prospective studies for the exact role of PERT in the pain of CP need to be done taking all the above facts into

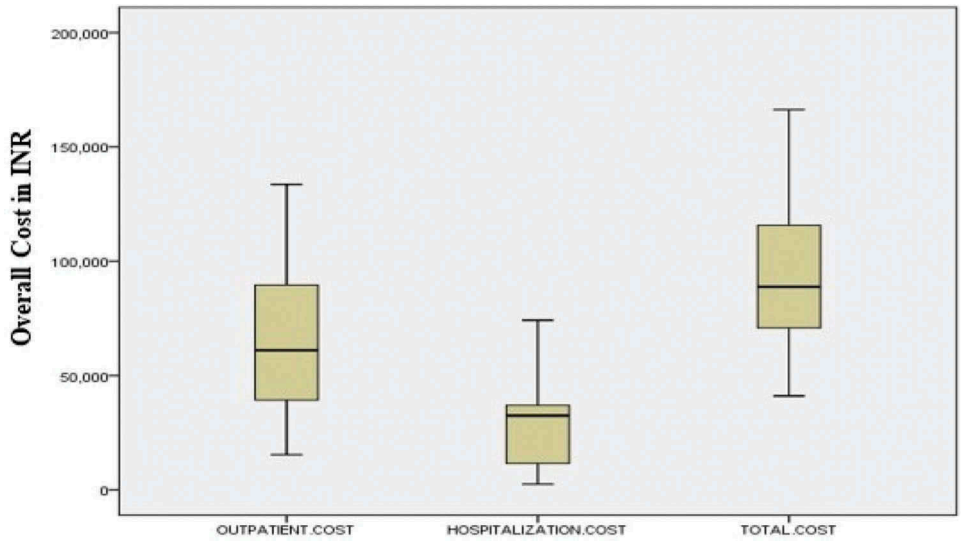

Figure 1. Box-plot diagram shows the minimum and maximum values (vertical lines), the averages and medians (numbers), and the interquartile ranges (box) showing median outpatient, hospitalization and total cost.

consideration are needed. Since PERT is expensive, patients should be told about drug cost and physicians need to prescribe the least costly alternative brand when available. PPIs result in nutritional deficiencies, increasing evidence of osteoporosis in CP with long-term use [28]. Hence, patient should be advised not to continue these drugs without medical supervision. No one PPI has been shown to be superior to another; however, esomeprazole or rabeprazole reduces the total cost by 3 and 4%, respectively, when given for 1 year as compared to pantoprazole.

The pain of CP not responding to drug therapy may be treated endoscopically or surgically. Costs per hospitalization were higher in patients who underwent ERCP than others in our study. Currently, only two randomized controlled trials are available for endotherapy versus surgery for CP both favoring surgery over endotherapy [29,30]. Both trials mentioned endotherapy has an initial role as first line of treatment, or as alternative for less extensive disease, with surgery being done when the former fails or recurrence of CP. Both the trials were criticized for a number of flaws including relatively small sample size [31]. One study had almost 3 times complication rate for surgery in CP versus that of endotherapy (29.8 vs. 10%) [32]. The only available pharmacoeconomic study for adult patients with CP had shown that surgical procedures were cost effective for all scenarios of CP [30]. However, ESGE guidelines recommend extracorporeal shock wave lithotripsy accompanied by endoscopic extraction of stone fragments for obstructive CP [33]. Hence, estimating the cost of nonsurgical therapy for CP assumes importance. The need of the hour is randomized controlled study in CP for endotherapy versus surgery for pain reduction including pharmacoeconomic components. The nonsurgical approach was effective for managing patients with CP in our study as seen in other community-based studies around the world [20,34–36].

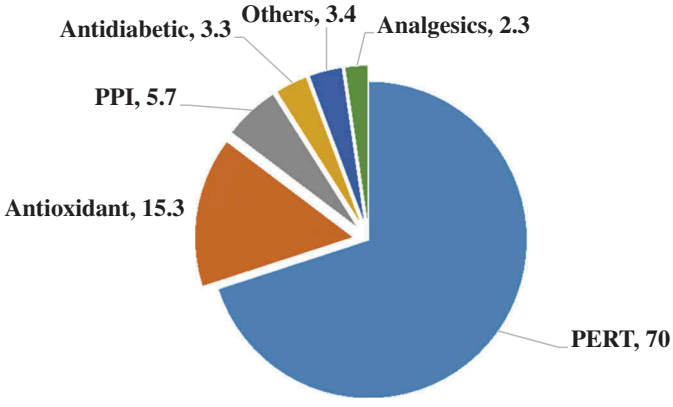

Figure 2. Breakdown of cost spent towards medicines.

Expenditure on healthcare may not be covered by health insurance in CP if they had past history of alcoholism as this is a clause of exclusion and patients have to bear the cost. Alcohol de-addiction costs also contributed to increased expenditure in CP. A clear relationship between alcoholics, diabetics, and increased cost in CP was demonstrated in our study. Patients should be advised to cut down on consumption of alcohol and quit smoking as they are the common etiological factors.

This pharmacoeconomic study is a modest outset in a developing middle-income country like India where such concepts of cost analysis are not common knowledge. The costs and proportional distribution between medication, hospital costs, investigation, and other treatments are different in our study than usually incurred in many western countries, especially the USA. This might be for healthcare services in the USA are expensive and about 85% higher than other OECD countries, though the former is acknowledged to have the best healthcare in the world [37]. In India, there is a common fee so healthcare services get paid a fixed amount for most of the patients being treated, whereas in the USA it depends on the health insurance policy. In India, the cost of outpatient treatment is not reimbursable under most schemes. Therefore, patient

needs to spend out of pocket to meet the expenses. Currently, a direct head to head cost comparison is not feasible, since just a single pediatric study exists on the cost of acute recurrent and CP which included surgical and endoscopic cost [38]. However, the cost of pancreatic cancer has been previously evaluated [39–42].

4.1. Limitations

In interpreting the results of our study, it is important to note some limitations which also include those stemming from the chosen pharmacoeconomic approach. Retrospective studies can miss clinical events and the level of evidence is low in comparison to prospective studies. We could calculate only direct costs; indirect costs were not estimated. These are obviously almost as important, given the years of productivity losses, cost of informal care provided by their family members and the intangible cost of grief and suffering would present as substantial economic burden which would further increase the total annual cost. COI studies are sensitive to regional variability. Not only do unit costs differ vastly between countries (and even regions, hospitals), but also demographics and other patient-related factors such as etiology. This study was conducted in a specialized unit of a tertiary care center and would have thus included a select band of referred patients with intractable disease, results (single centered) of which may not be generalizable outside of this environment. Some patients were asked to follow up telephonically after a procedure who could not come for scheduled follow up. The resultant cost savings has not been estimated. Continuing the study prospectively over a longer period would have provided more robust results. Despite these pitfalls, our findings contribute greatly to the pharmacoeconomics of CP which has remained unexplored around the world till now.

5. Conclusion

To summarize, the direct cost in CP are driven by drugs and hospitalization and managing the condition is a costly affair. To the best of our knowledge, our study is the first in the world to calculate the direct cost for nonsurgical management in CP. Future prospective evaluation will help to determine the direct and indirect costs more precisely. Given the magnitude of the costs, results from our study do pave the way for future studies as well raise cognizance about the necessity for streamlining cost effective treatment measures for CP.

Key issues

- Chronic pancreatitis is a progressive illness with persistent inflammation of the pancreas which needs quick assessment and appropriate medical therapy
- Direct cost borne by patients with Chronic pancreatitis was previously unexplored
- Educating patients on compliance with drug therapy and proper follow-up with one gastroenterologist may provide substantial cost savings
- Indirect costs are difficult to measure, however needs to be estimated in future studies
- Interventions focusing on patient awareness of cost in chronic pancreatitis and improving the quality of life must be a public health priority

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Declaration of Interest

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties. Peer reviewers on this manuscript have no relevant financial or other relationships to disclose.

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Conflicts of interest

None to disclose.

Authors' contributions

Nagesh Kamat (NK), Surulivel Rajan Mallayasamy (SRM), Ganesh Pai (GP) designed the study. NK collected data, performed statistical analyses along with Asha Kamath (AK) and interpreted the results with Rajasulochana S (RS). NK drafted the article. SRM, AK, RS and GP provided vital inputs. The final manuscript was reviewed and approved by all the authors.

Compliance with Ethical Standards

For this type of study, formal consent is not required, however our study received institutional ethics committee approval.

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