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TITLE: The efficacy of Magnetic resonance cholangiopancreatography in assessing the etiology of acute idiopathic pancreatitis

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ABSTRACT

Aims:
Idiopathic pancreatitis may be diagnosed once all causes of pancreatitis are excluded by thorough history, metabolic profile and conventional imaging modality i.e. abdominal ultrasonography. In this study we have attempted to evaluate the cause of idiopathic pancreatitis with the help of MRCP.

Methods:
Fifty patients presenting with idiopathic pancreatitis were assessed prospectively using MRCP with strength 1.5 T for potential cause of the attack of pancreatitis.

Results:
Fifty patients presenting with idiopathic pancreatitis were assessed with MRCP. MRCP was able to establish the cause of pancreatitis in eleven (22%) patients, as follows. CBD stone in one (2%), Pancreatic divisum in one (2%), GB stone in one (2%), pancreatic duct stone in one (2%), chronic pancreatitis in two (4%), GB sludge in two (4%) and anomalous pancreaticobiliary union in three (6%) patients.

Conclusion:
MRCP, a non invasive and complication free imaging modality is able to establish the cause of acute pancreatitis in patients in whom the diagnosis of idiopathic pancreatitis has been made following standard investigations. Idiopathic pancreatitis should not be diagnosed unless MRCP has been performed.

Keywords: Idiopathic Pancreatitis, Pancreatitis, Causes of Pancreatitis, MRCP
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INTRODUCTION

Acute pancreatitis is a common disease that causes significant morbidity and mortality throughout the world. The commonest etiological factors for AP are cholelithiasis and alcohol (70-75%) [1]. Other less common causes for AP include iatrogenic causes such as (ERCP) endoscopic retrograde cholangiopancreatography, abdominal surgery, trauma, hypertriglyceridemia, hypercalcemia, drug induced, autoimmune, genetic, ischemic, various infections, congenital pancreatic divisum, Microlithiasis / sludge. Determining the cause of pancreatitis is an essential component of diagnostic evaluation. Since, the cause guides the management thereby allows elimination of precipitant and prevention of disease recurrence. Besides this, different causes have different natural histories with different complications (e.g. alcohol versus biliary pancreatitis). Furthermore, certain causes of pancreatitis have long-term consequences (e.g. pancreatic cancer associated with hereditary pancreatitis).

Apart from routine evaluation for the cause of pancreatitis e.g. serum Amylase, serum Calcium and triglyceride levels, abdominal ultrasonography, an unexplained pancreatitis should be evaluated aggressively as there can be grave consequences associated with idiopathic pancreatitis. Idiopathic Pancreatitis forms the largest subgroup (40%) of all acute pancreatic fatalities [2], [3]. Furthermore, over 50% of untreated patients with acute idiopathic pancreatitis experience recurrence [4-6], recurrent pancreatitis may progress to chronic pancreatitis with irreversible morphologic and functional changes [7], [8]. Repeated hospitalization for pancreatitis is also associated with loss of health care resources. On initial negative evaluation other investigations including ERCP, MRCP and sphincter of Oddi manometry may be used. In this study we have attempted to evaluate the patients of idiopathic pancreatitis with MRCP, which is non invasive and apparently complication free imaging modality.

MRCP is a non-invasive imaging technique that does not involve exposure to ionizing radiation. It can produce images comparable to those obtained by invasive
investigations such as ERCP without its associated risks including pancreatitis, perforation of biliary or pancreatic ducts or bowel perforation and risks of intravenous contrast agents required for ERCP. MRCP uses heavily T2-weighted sequences by which the signal of static or slowly moving fluid in structures such as biliary and pancreatic ducts is greatly increased leading to increase in duct-to-background contrast. MRCP can be used to investigate the cause of idiopathic pancreatitis in a non-invasive manner.

MATERIALS AND METHODS

The study was conducted by Deptt. Of Gastroenterology at tertiary care hospital from May 2011 to Oct 2013. During this period 355 patients were admitted in the deptt. with diagnosis of pancreatitis on the basis of history, physical findings, evidence of elevation of serum amylase level. Amylase level of three fold the upper limit of normal serum level was taken as significant to qualify for diagnosis of pancreatitis and abdominal ultrasonography (US)).

In three-hundred (84.5%) patients cause of pancreatitis could be established, based on history, metabolic profile (Hypercalcemia, Hypertriglyceridemia) and US abdomen (Table 1). In rest of fifty-five (15.5%) pancreatitis patients cause could not be determined. Therefore fifty-five patients were diagnosed as Idiopathic pancreatitis. Of these Idiopathic Pancreatitis patients five patients were excluded from the study because of following reasons. Two patients because of claustrophobia, two patients did not give consent and one had the contraindication to MRCP in the form of permanent pacemaker implantation, hence, our study population of Idiopathic Pancreatitis comprised of 50 patients. Inclusion criteria included patient with idiopathic pancreatitis and written informed consent for study, exclusion criteria consisted of Patients with absolute contraindication to MRCP, alcoholics, abdominal trauma, Post ERCP, family history of pancreatitis, recent offending drug intake, hypercalcemia, hypertriglyceridemia, severe sepsis.

Idiopathic pancreatitis was defined as wherein cause of pancreatitis could not be established on thorough history, metabolic profile, x-ray abdomen and abdominal ultrasonography. For further assessment of etiology fifty patients with idiopathic pancreatitis were subjected to MRCP.
MRCP was performed with 1.5T (Siemens, Germany) with a phased array multicoil. All sequences were performed during breath holding for 12 seconds. Heavily T2-weighted sequences were obtained in the coronal and axial planes. MRCP was interpreted prospectively by two experienced radiologists in relation to detectable abnormalities. Data was analyzed in SPSS 11.17 with respect to detectable abnormalities.

RESULTS

Fifty patients with idiopathic pancreatitis (IP) were studied. Twenty-two (44%) males and twenty-eight (56%) females with the age ranging from 15 -75 yrs, mean age of 44yrs. All these patients presented with two main symptoms, pain abdomen in 80% and combination of pain and vomiting in 20%. For further assessment of etiology of pancreatitis, fifty patients with IP were subjected to MRCP. MRCP was able to detect the cause of pancreatitis in eleven (22%) out of fifty patients of IP which are as follows (Chart 2).

In one (2%) out of fifty patients of IP, stone was evident as a dark filling defect at lower end of CBD which was retrieved at ERCP and endoscopic sphincterotomy (Figure 1).

In one (2%) out of fifty patients of IP, complete pancreatic divisum was diagnosed at MRCP. She was managed conservatively and is on follow-up from last 20 months without any further episodes of pancreatitis (Figure 2).

Gall stone was detected in one (2%) of fifty IP patients which was confirmed at subsequent cholecystectomy (Figure 3).

In one (2%) out of fifty patients of IP, a solitary stone in the pancreatic duct was detected at MRCP (Figure 4).

In two (4%) out of fifty patients of IP, MRCP appearances were consistent with chronic pancreatitis, the changes were consistent with early chronic pancreatitis, in these patients we will have to rely on observation over a long period of time than the 16-18 months follow up currently available.

GB sludge, was diagnosed in two (4%) out of fifty patients of IP which latter underwent Laproscopic cholecystectomy.
In three (6%) out of fifty patients of IP Anomalous pancreaticobiliary union (APBU) was diagnosed at MRCP, one of patients among three underwent endoscopic sphincterotomy, in view of frequent episodes of pancreatitis.

In rest thirty-nine (78%) IP patients, MRCP changes consistent with acute pancreatitis (edematous pancreas) were identified, without any cause. MRCP detected the cause of acute pancreatitis in eleven (22%) out of fifty IP patients.

**DISCUSSION**

In upto 10% of patients with a single episode of acute pancreatitis and in 30% of patients with acute recurrent pancreatitis etiology is not found after initial evaluation [9], [10]. It is recognized that further evaluation of patients with idiopathic pancreatitis may disclose evidence of potential etiology, such as unrecognized gallstone disease, CBD stone, chronic pancreatitis, APBU so that subsequent definitive management can be offered to the patients in order to prevent the morbidity and mortality associated with pancreatitis. In our study which comprised of fifty patients of idiopathic pancreatitis we attempted to assess the utility of MRCP in evaluating the cause of idiopathic pancreatitis.

MRCP is a non-invasive exploration which has also proved its value in diagnosing entities responsible for an attack of acute pancreatitis such as choledocholithiasis [11], [12], chronic pancreatitis, pancreatic duct strictures or stones, sphincter of Oddi dysfunction and anatomic anomalies [13-17].

The diagnostic accuracy of MRCP for choledocholithiasis is very high ranging between sensitivity 81-95% and specificity 85-98% as reported by several studies and with positive predictive value and negative predictive value from 82-100% and 94-100% respectively. Despite the accuracy of sonography and CT, these imaging modalities are inferior to MRCP in diagnosis of choledocholithiasis [12-14]. Moon JH et al in his study on bile duct stones in suspected biliary pancreatitis revealed that overall agreement between MRCP and ERCP was 90.6% for detection of bile duct stones and concluded that MRCP can be used to select patients with biliary pancreatitis who require ERCP for intervention [18]. Mc Mohan et al while evaluating the relative roles of MRCP and EUS in investigating CBD calculi “evidence based
practice" methods concluded MRCP should be the first line of investigation of CBD calculi [19]. The frequency and morbidity of recurrent pancreatitis are great, as undiagnosed biliary disease carries a recurrence rate of 20-50%, whereas the risk of recurrent pancreatitis associated with biliary stones decreases to less than 5% after corrective surgery [21].

Choledocholithiasis detected in one (2%) out of fifty IP patients was latter confirmed at ERCP and subsequent stone extraction. Pancreatic divisum occurs as an anatomic variant in 5% - 7.5% of patients (5, 21). At MRCP one (2%) out of fifty IP patients was diagnosed to have complete pancreatic divisum in our study. Bret et al has shown that MRCP has 100% accuracy for the detection of pancreatic divisum [16]. In the past pancreatic divisum was established with ERCP. However, because of risk of inducing or exacerbating pancreatitis, MRCP is preferred in the evaluation of pancreatitis with suspected pancreatic divisum.

Gallstone in one (2%) out of fifty IP patients was detected at MRCP in our study which was confirmed at subsequent cholecystectomy. One (2%) out of fifty IP patients was diagnosed as having pancreatic duct stone seen as dark round filling defect surrounded by high signal intensity pancreatic fluid. Recently, magnetic resonance cholangiopancreatography (MRCP) has been used for diagnosing chronic pancreatitis [22]. Sugiyama M et al, in his study showed that MRCP well demonstrates dilatation, stricture and irregularity of MPD as well as filling defects due to stones and protein plugs in chronic pancreatitis [23]. Hever Hagen JT et al concluded that secretin administration further enhances MRCP value for diagnosis of chronic pancreatitis. He showed that secretin administration not only improves the visibility of pancreatic duct but also its side branches thereby increasing the diagnostic accuracy of MRCP in chronic pancreatitis [24]. Therefore MRCP may be useful for diagnosis of chronic pancreatitis. In our study, we diagnosed two (4%) out of fifty IP patients as having chronic pancreatitis which was of mild grade as per Cambridge classification.

In our study two (4%) out of fifty IP patients MRCP identified biliary sludge as a cause of pancreatitis, these patients latter underwent laparoscopic cholecystectomy. Biliary lithiasis is an important cause of morbidity throughout the world. Ultrasound is
the diagnostic method of choice in such patients as it is rapid, non-invasive, highly sensitive and specific (>95%) in establishing the presence and absence of gallbladder stones more than 2mm in diameter [25], [26].

Biliary sludge is sometimes difficult to diagnose and represents the cause of more than half of all cases of acute idiopathic pancreatitis [10], [27-29]. In these cases invasive procedures are required such as duodenal catheterization, ERCP mediated bile aspiration [30].

Anomalous union of the pancreatic and bile ducts is seen in 1.5%-3% of individuals. The union is characterized by an unusually long (>15mm) channel common to the two ducts that lies proximal to the sphincters of the pancreatic and bile ducts in the duodenal wall. Because the action of the sphincter does not functionally affect the union, two-way regurgitation occurs and allows reflux of bile into the pancreatic duct. This results in frequent attacks of pancreatitis. The diagnosis of pancreaticobiliary malformation is confirmed by visualizing the biliary and pancreatic ductal systems on ERCP. Currently MRCP is becoming one of the first choices in evaluation of pancreaticobiliary malformation in a non-invasive manner [24], [27]. MR cholangiopancreatography allows complete anatomical analysis of whole pancreaticobiliary tree to precise the size and morphological characteristic of CBD (sensitivity 100%) and for pancreaticobiliary malformation (sensitivity 69%) hence may replace the ERCP for diagnostic evaluation [31]. The study performed on 32 subjects by Kamisava et al concluded that conventional MRCP is quite useful tool for diagnosis of congenital pancreaticobiliary malformation though diagnostic accuracy can be enhanced with 3 – dimentional MRCP or MRCP with secretin administration [32]. In our study diagnosis of APBU was made at MRCP in three (6%) of fifty IP patients in the form of long common channel with 16mm, 16.5mm and 18mm as dimensions. One of these patients had multiple episodes of pancreatitis, since he was diagnosed, who underwent endoscopic sphincterotomy latter.

In one (2%) out of fifty IP patients in our study suffered from repeated episodes of pancreatitis the patient was subjected to ERCP and stone was retrieved out ampullary area.

In Thirty-nine (78%) out of fifty IP patients MRCP could not detect any cause of pancreatitis. We assume that many of these patients would have ascariasis as cause
of pancreatitis, as worm infestation is highly prevalent in this part of world, since ascariasis induced pancreatitis was shown to have incidence of 23% by khuroo et al in his study [33]. By the time MRCP was done worms would have been already out of biliary and pancreatic ducts. Furthermore, evaluation for SOD, bile aspiration for biliary sludge, genetic studies or autoimmune pancreatitis may be needed to establish the etiology in remaining cases.

Alcohol induced pancreatitis was quite less (1.4%) in our study as compared to reported in world literature, the reason is obvious since alcohol consumption is very little in this part of the world due to cultural and religious implications.

CONCLUSION
As knowledge and technology advances, the true idiopathic pancreatitis is declining. Since, elucidation of cause of pancreatitis now-a-days has become more obvious with the advancement of laboratory and imaging studies. Establishing etiology with a non-invasive MRCP could have a substantial effect on the management of acute idiopathic pancreatitis as it guides about the treatment, thereby reducing the morbidity and mortality associated with pancreatitis. MRCP is relatively new diagnostic technique with several advantages over other invasive and non-invasive methods of imaging biliary and pancreatic ductal systems in pancreatitis. MRCP is a promising tool for evaluating the patients with idiopathic pancreatitis as it is able to detect pathology in these patients even when standard imaging is unsuccessful. Therefore, we recommend the use of MRCP in pancreatitis before labeling it as an Idiopathic pancreatitis.

CONFLICT OF INTEREST
We have no conflict of interest to declare.

AUTHOR’S CONTRIBUTIONS
Prof. Yattoo GN
Group 1 – Substantial contributions ton conception and design, acquisition of data
Group 2 – Drafting the article, revising it critically for important intellectual content
Group 3 – Final approval of the version to be published
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Group 2 – Drafting the article, revising it critically for important intellectual content
Group 3 – Final approval of the version to be published

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REFERENCES


### Table 1: Etiological profile of 355 patients of pancreatitis.

<table>
<thead>
<tr>
<th>Etiology of Subjects</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gallstone</td>
<td>256</td>
<td>72.0%</td>
</tr>
<tr>
<td>Worm induced</td>
<td>15</td>
<td>4.2%</td>
</tr>
<tr>
<td>Chronic pancreatitis</td>
<td>12</td>
<td>3.4%</td>
</tr>
<tr>
<td>Post ERCP</td>
<td>8</td>
<td>2.2%</td>
</tr>
<tr>
<td>Alcohol</td>
<td>5</td>
<td>1.4%</td>
</tr>
<tr>
<td>Hypercalcemia</td>
<td>4</td>
<td>1.1%</td>
</tr>
<tr>
<td>idiopathic</td>
<td>55</td>
<td>15.5%</td>
</tr>
<tr>
<td>Total</td>
<td>355</td>
<td>100%</td>
</tr>
</tbody>
</table>

### Table 2: Frequency distribution of various etiologies detected at MRCP.

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>IDIOPATHIC</td>
<td>39</td>
<td>78.0%</td>
</tr>
<tr>
<td>APBU</td>
<td>3</td>
<td>6.0%</td>
</tr>
<tr>
<td>CHRONIC PANCREATITIS</td>
<td>2</td>
<td>4.0%</td>
</tr>
<tr>
<td>PANCREATIC DIVISUM</td>
<td>1</td>
<td>2.0%</td>
</tr>
<tr>
<td>CBD STONE</td>
<td>1</td>
<td>2.0%</td>
</tr>
<tr>
<td>MPD STONE</td>
<td>1</td>
<td>2.0%</td>
</tr>
<tr>
<td>GB SLUDGE</td>
<td>2</td>
<td>4.0%</td>
</tr>
<tr>
<td>GALL STONE</td>
<td>1</td>
<td>2.0%</td>
</tr>
<tr>
<td>Total</td>
<td>50</td>
<td>100.0%</td>
</tr>
</tbody>
</table>
FIGURE LEGENDS

Figure 1: 38yr old female with CBD stone.
Figure 2: 47yr old female pancreas. Divisum.
Figure 3: 34yr old female with MPD stone.
Figure 4: MrCP showing GB stone in 41yr male.
Figure 5: Showing GB Sludge in 39yrs Female.
Figure 6: Long common channel in 18yr male.

FIGURES

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Figure 2: 47yr old female pancreas. Divisum.

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