



ASIAN INSTITUTE OF GASTROENTEROLOGY AT DDW 2019, SAN DIEGO

Invited lectures

ASGE Post Graduate Course

Conquering difficult bile stones

D. Nageshwar Reddy

American Bariatric Endoscopy Group

Bariatric Endoscopy in South East Asia

D. Nageshwar Reddy

ASGE/SGEI Session

Advances in interventional EUS

Sundeep Lakhtakia

Distinguished Plenary Session (Pancreas section) oral presentations

Impact Of Personalized Counseling On Depression And Quality Of Life In Patients With Chronic Pancreatitis: Results From A Randomized Controlled Trial.

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Background: Chronic pancreatitis (CP) is associated with depression & poor quality of life. We earlier reported that continuous & severe pain determines development of depression & depression adversely impacts quality of life (QOL) components (*Oral presentation at DDW 2018*). In this intention-to-treat, pilot randomized controlled trial we evaluated impact of personalized counseling on depression, QOL and symptoms in patients with CP.

Methods: We recruited 63 patients with CP and depression, randomized 33 of them into personalized counseling and 30 into the control arm. Figure 1a depicts the personalized counseling protocol. Primary outcome was reduction in depression score, while secondary outcomes were improvement in QOL, downgrading in the categories of depression, and impact on pain.

Following parameters were recorded at enrollment: demographic variable, pain details in past 3 mths, other disease characteristics, morphology, and treatment details. Depression was measured using the Beck depression inventory (BDI) while quality of life was evaluated using the EORTC-QLQ-30 with PAN28 at baseline and repeated after 3 months. Pain parameters were also measured at the end of 3 months.

We performed magnetic resonance spectroscopy (MRS) in another 14 patients using the 1.5 T MR scanner using 2D-PRESS at Echo Time (TE)-14 m second and Repetition Time (TR)-2 sec in the Pre Frontal cortex (PFC), Basal Ganglia (BG), Hippocampus (H) and Anterior Cingulate Cortex (ACC) for the metabolites Glutamate/Glutamine (Glu/Gla), Myoinositol, N-acetyl aspartate (NAA) and Creatine. Plasma metabolites were measured by GC-MS/MS using the Shimadzu GC2010 plus system.

Results: There were no differences in the baseline characteristics between the study groups. None of the patients received high potency narcotics or anti-depressants. Mean (95% CI) counseling time was 38 (32-43) minutes. At the end of 3 months, there was a significant reduction in mean (95% CI) BDI score among patients who received counseling (9.1 [6.01-12.1] vs 18.0 [10.9-25.1]; $p < 0.0001$) (Fig 1b). There was downgrading in the category of depression among counseled patients. We also observed improvement in the mean (95% CI) emotional and cognitive components of the EORTC-QLQ30 (46.6 [39.4-53.8] vs 27.9 [18.6-37.1]; $p = 0.001$ and 77.6 [70.8-84.3] vs 60.8 [46.2-75.4]; $p = 0.03$, respectively) (Fig. 1c, 1d). Interestingly, there was also a trend towards improvement in the mean (95% CI) pain score post-counseling (5.2 [4.2-6.2] vs 6.6 [6.0-7.2]; $p = 0.07$).

There was a significant difference in the metabolite peak heights between moderate and severe depression of Glu/Gla and creatine in the hippocampus and basal ganglia, and myoinositol in the basal ganglia (Fig. 2a-e). There were no differences in the plasma metabolite profile.

Conclusion: Personalized counseling improves depression and QOL parameters, which could be mediated by altered brain metabolites.

Fig. 1a

Steps of the counseling protocol:

1. Greetings and informed consent.
2. Recording clinical data and administering questionnaires.
3. Explaining the disease and possible outcomes in the context of the clinical data.
4. Answering queries from patient and their domestic caregivers.

Fig. 1b

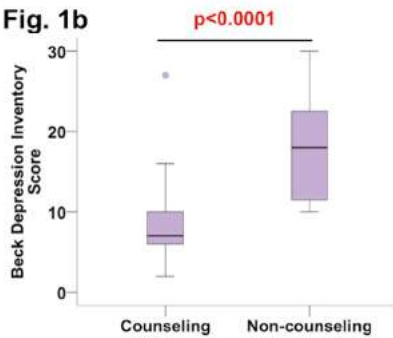


Fig. 1c

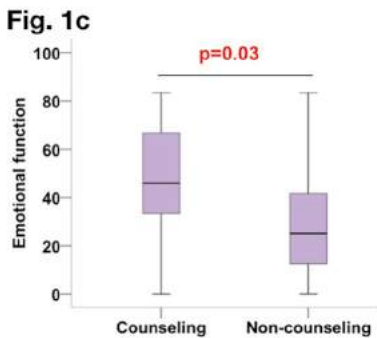


Fig. 1d

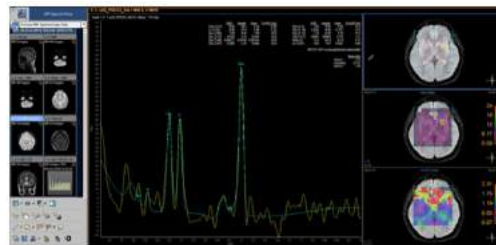
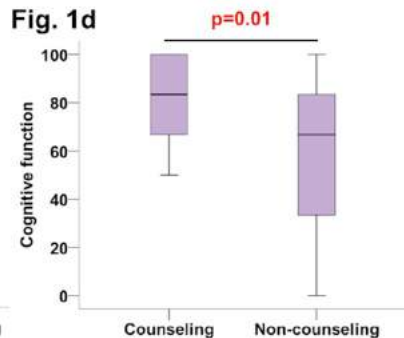


Fig. 2a: Representative MRS image of patient with severe depression

Fig. 2b: Glu/Gla

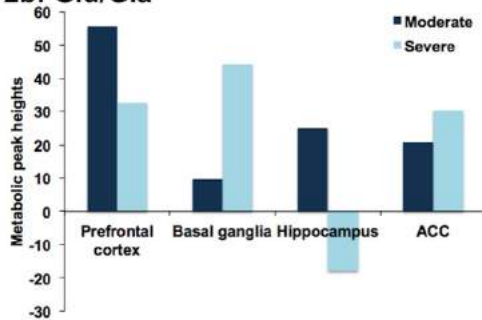


Fig. 2c: Creatine

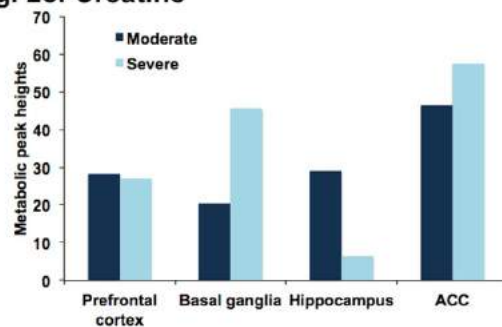


Fig. 2d: Myoinositol

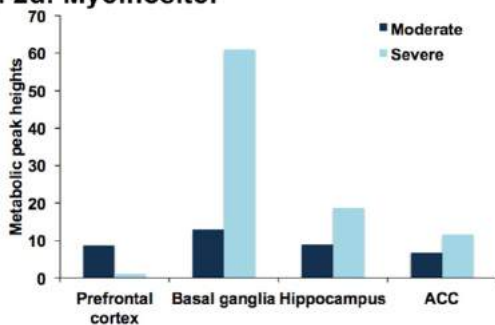
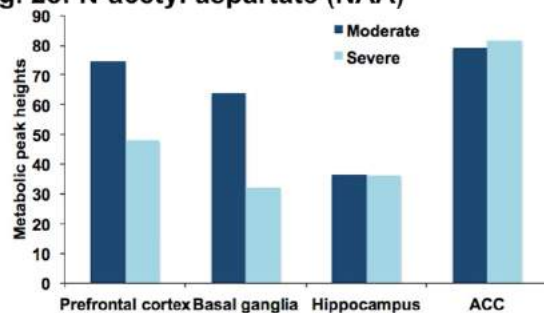


Fig. 2e: N-acetyl aspartate (NAA)



Research forum oral presentations

Dynamic Association Of Systemic Inflammation, Gut Microbial Dysbiosis And Gut Barrier Integrity In Acute Pancreatitis (Ap): Lessons Learnt From Animal Model.

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Introduction: Infected pancreatic necrosis(IPN) in AP raises mortality and morbidity substantially. The source of IPN is the gut flora. RCTs testing prophylactic antibiotics have failed to prevent IPN. Even though SIRS and intestinal barrier integrity in AP have been studied independently, the dynamic interactions among these events and gut microbial dysbiosis are still speculative.

The aim of this study was to evaluate the association between pancreatic & intestinal inflammation, intestinal microbial dysbiosis and altered gut barrier function in AP in a time dependent manner.

Methods: AP was induced in C57Bl/6J mice with 10 hourly intra-peritoneal injections of caerulein (50µg/kg). Fecal pellets were collected at baseline, 12, 24, 48 & 72hrs and metagenomic DNA was isolated from fecal pellets. V3-V4 regions of 16SrDNA were sequenced to study the variations in the gut microbial population. Animals were sacrificed at different time points (12, 24, 72hrs) after AP induction. Pancreatic and small intestine tissues were harvested to perform biochemical, histological and expression(mRNA, protein) studies. Trypsin activity in pancreatic tissue was quantified using Kawabata's method. Histological changes in pancreatic and intestinal tissues were observed and scored. Systemic and tissue (pancreatic, ileal) infiltrated cytokines concentration were quantified by using FACS. Altered intestinal permeability was identified by performing qRT-PCR and IHC studies for ZO-1, ZO-2 and occludin. Intestinal epithelial cell apoptosis were identified and quantified by IHC for caspase-3.

Results: Successful induction of AP was confirmed by elevated trypsin activity and inflammatory changes in pancreatic tissue, which was maximum at 12hrs. Circulating IL-6 and TNF-α were significantly elevated at 12hrs of AP induction, indicating SIRS. Besides inflammation, pancreatic & ileal tissue homogenates also showed increased IL-6 and TNF-α concentration at 12 hrs (Fig. 1a,b). mRNA expression studies and immunohistochemistry in intestinal tissue showed significant down-regulation of tight junction protein ZO-1, ZO-2, occludin, which reached lowest level at 72hrs (Fig 1c,d). IHC in intestinal epithelial cells showed significantly increased caspase-3 expression at 24hrs (Fig 1e). Principal component analyses (PCA) and hierarchical clustering of metagenomic data confirmed presence gut microbial dysbiosis in AP induced mice (Fig 2 a,b). Relative abundance of phylum Bacteroidetes and genus Bacteroides were significantly elevated after 48hrs of AP induction.

Conclusion: We observed a time dependent intestinal inflammation, gut microbial dysbiosis and altered gut permeability during early phase AP (Fig. 2c,d), which could further cause bacterial translocation and result in infected necrosis. Our data raises the possibility of gut microbial manipulation as potential modality to prevent IPN.

Fig. 1a: Ileal inflammation

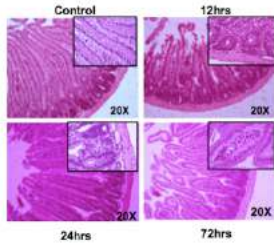


Fig. 1b: Quantification of ileal inflammation

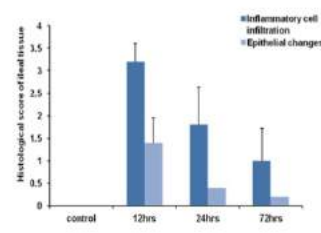


Fig. 1c: mRNA expression of gap junction proteins

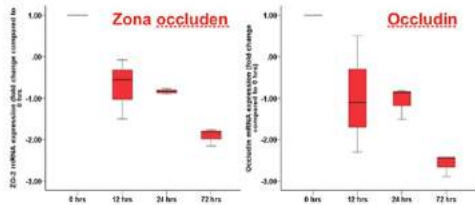


Fig. 1d: IHC showing Zona expression

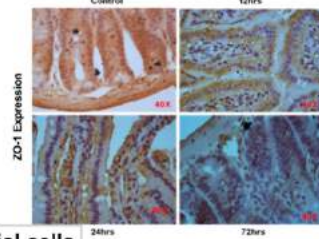


Fig. 1e: Apoptosis of epithelial cells

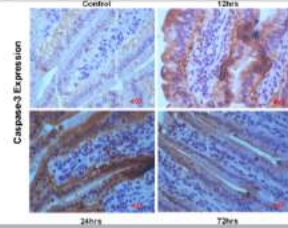
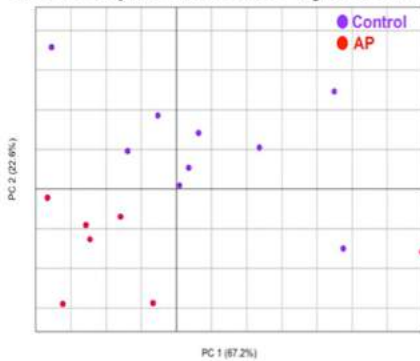
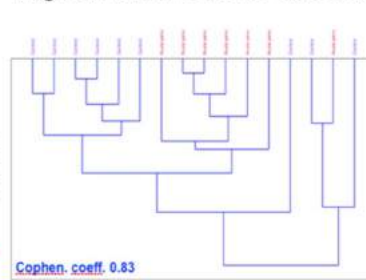


Fig. 2a: PCA to depict microbial dysbiosis



Principal coordinate analysis (PCA) of gut microbial genus abundance

Fig. 2b: Hierarchical clustering



Dendrogram showing hierarchical cluster analysis

Fig. 2c: Time dependent events

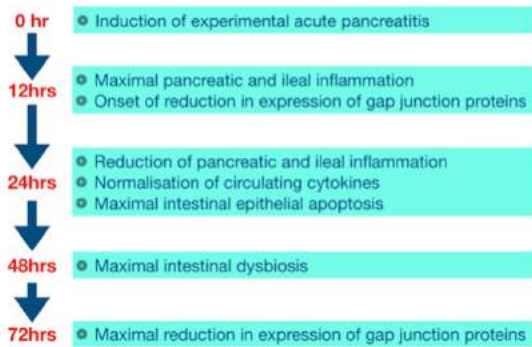
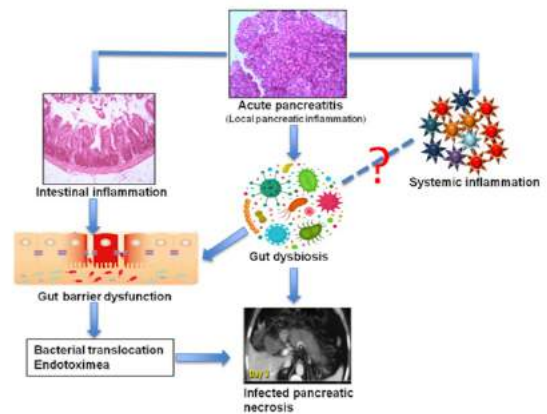


Fig. 2d: Hypothesis



Transcriptome Analysis During Progression Of Chronic Pancreatitis Identifies Sequential Receptor Alterations.

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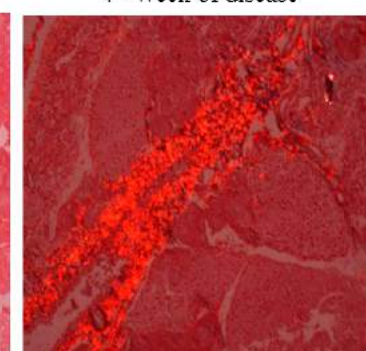
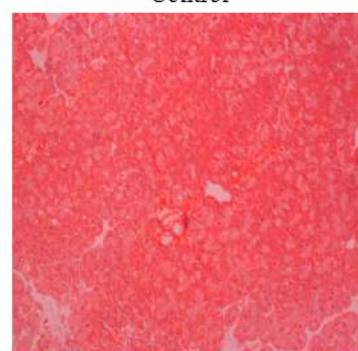
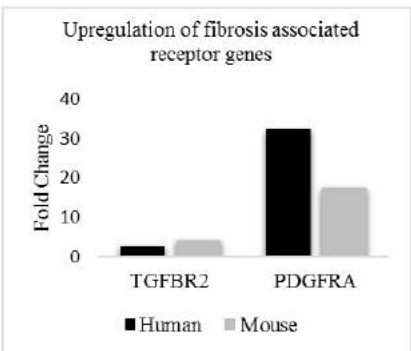
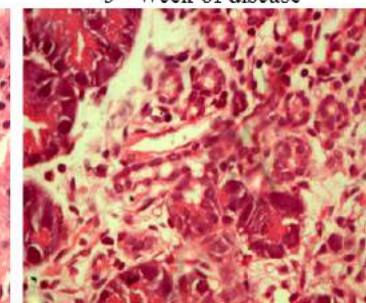
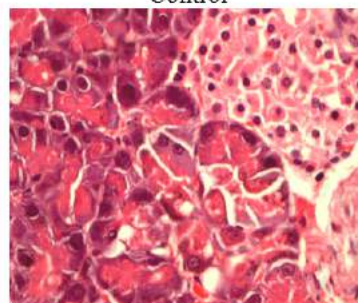
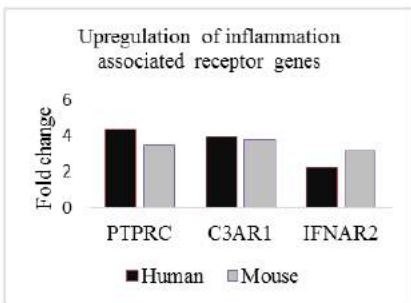
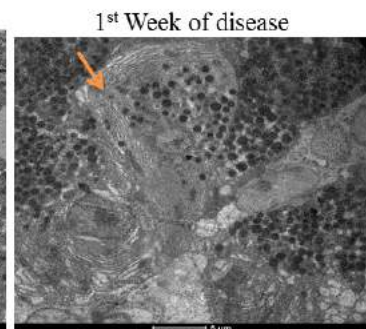
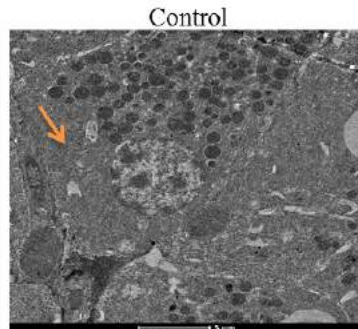
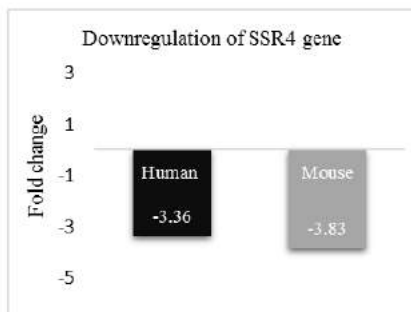
Introduction: Elucidation of molecular and cellular events during progression of pancreatitis, from acute injury to replacement of pancreatic parenchyma with fibrosis concomitant with exocrine/endocrine deficiency, would aid in developing novel strategies for its management. We performed transcriptome analysis during progression of arginine-induced Chronic Pancreatitis (CP) in mice and correlated with transcriptome data obtained from patients diagnosed for chronic pancreatitis and features of CP during disease progression.

Methods: Pancreatic tissues from human cadavers and CP patients undergoing surgery as well as from mice with L-arginine induced CP, were subjected to Affymetrix Human Transcriptome Arrays 2.0 and Affymetrix Clariom D mouse Array respectively. Global gene expression was obtained using transcriptome analysis console software v3.0. The receptor expression in human CP and in mice pancreatitis for 4 weeks were compared, to identify common receptors involved in progression of pancreatitis in mice and humans. Altered cellular events during progression of the disease were monitored employing Electron microscopy, histological examination and flow cytometry.

Results: Transcriptome analysis revealed similar pattern of 139 genes out of 369 dysregulated genes, which includes genes coding for receptors, hormones, fibrosis, inflammation, redox balance and splicing factors. Enlarged endoplasmic reticulum (ER), enhanced expression of GRP68, a marker of ER stress was noted along with Signal Sequence receptor 4 (SSR4) downregulation in the first week both in mice (-3.83) and human CP (-3.36 fold). Lymphocyte infiltration noted in the third week was accompanied with enhanced expression of PTPRC [involved in T cell activation, both in humans (4.34 fold) and in mice (3.5 fold)] and that of NR4A1 [associated with inflammation, both in humans (19.68) and in mice (2.24 fold)], followed by downregulation of NR5A2 [involved in acinar cell differentiation correlating with loss of parenchyma, in humans (-4.17 fold) and in mice (-5.86)]. Progression of the disease in the fourth week was associated with upregulation of C3AR1 [involved in chemotaxis and oxidative stress in humans (3.99) and in mice (3.79)] and that of IFNAR2 [associated with STAT activation in humans (2.24 fold) and in mice (3.17 fold)] correlating with increased oxidative stress and increased TNF- α expression. Increased thickening of collagen fibres (from $8.9 \pm 3.01 \mu\text{m}$ at the 2nd week to $25.6 \pm 5.87 \mu\text{m}$ at the 4th week) coincided with the upregulation of TGFBR2 in human (2.8 fold) and mice (4.28 fold) & PDGFRA in human (32.6 fold) and mice (17.64 fold).

Conclusion: The sequential alterations in the receptor gene expression correlating with features of CP may be studied as potential therapeutic drug targets.

Association of receptor expression with features of chronic pancreatitis



Posters (including posters of distinction*)

* **Metabolomic Profiling Identifies Phospholipid Signature In The Progression Of Diabetes In Chronic Pancreatitis**

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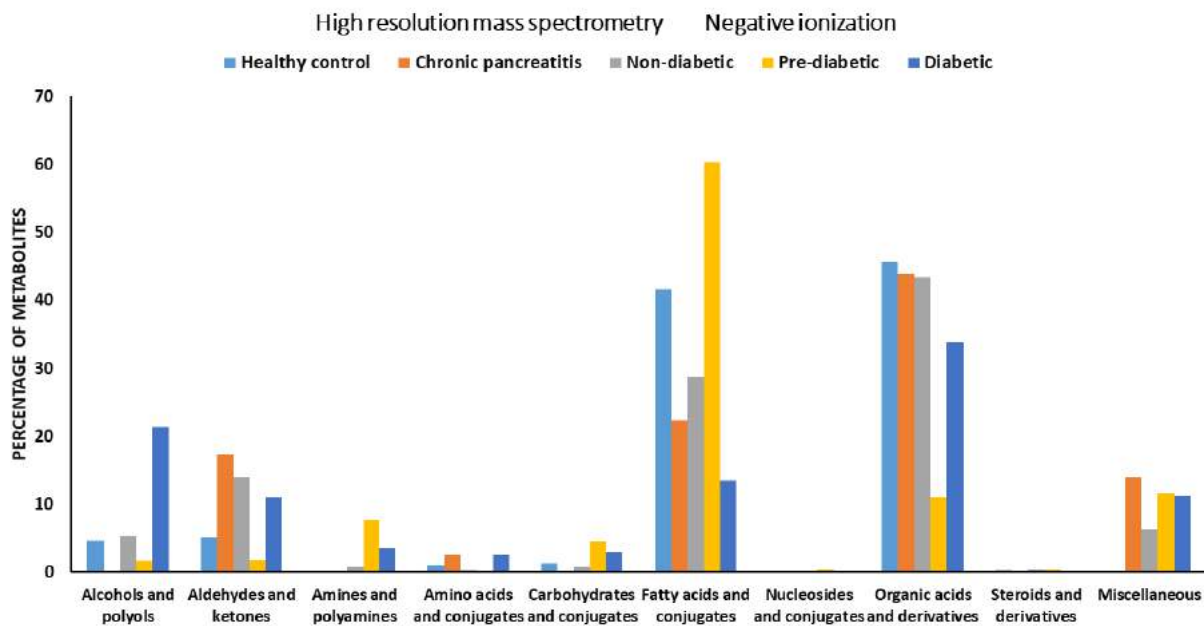
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Introduction: Altered glucose metabolism in chronic pancreatitis (CP) ranges from mild impairment of β -cell dysfunction to severe form, characterized by frequent episodes of iatrogenic hypoglycemia. Understanding progression from mild to severe form is essential to predict the development of Type 3c diabetes (T3cDM) from the state of normal glucose tolerance through prediabetes. As metabolic dysregulation occurs in CP, we evaluated metabolomic profiles during progression to identify prediabetes markers.

Methods: Patients diagnosed with CP (n=210) and non-diabetic healthy volunteers (n=30) were subjected to oral glucose tolerance test (OGTT) and whole blood was collected for metabolomic profiling. Polar and non-polar metabolites were isolated from plasma and untargeted metabolomic profiling was performed with high-resolution tandem mass spectrometry. Bioinformatics tools applied to m/z peaks and metabolites were identified from human metabolome database. Upon identification, targeted profiling was performed to quantify the metabolites using LC-MS Q-TOF. Data was analyzed by descriptive statistics and receiver operating characteristic.

Results: OGTT categorized CP patients into three groups; nondiabetic (41%), prediabetic (35%) and diabetic (24%). Untargeted metabolome profiling identified alcohols, amino acids, fatty acid conjugates and organic acid derivatives as major metabolites. Among these, noticed significant variation of fatty acid conjugates (phospholipids) in 28% nondiabetic, 60% prediabetic and 12% diabetic of CP patients and further quantification focused on phospholipids for targeted metabolome profiling. LysoPE(0:0/20:4(8Z, 11Z, 14Z, 17Z)) a phosphatidylethanolamine, PA(8:0/15:0)/PA(10:0/a-13:0), phosphatidic acid and O-adipoyl carnitine (transfer of fatty acids and phospholipids) were identified only in CP patients. O-adipoyl carnitine detected only in nondiabetic and prediabetic CP patients showed 100% specificity, 50% sensitivity with AUC (82%, $p=0.001$). Phosphatidic acid detected only in prediabetic and diabetic patients showed 92.3% sensitivity, 27% specificity with AUC (56.4%, $p=0.5$). LysoPE detected among all the sub groups, showed 80% sensitivity, 57% specificity with AUC (65%, $p=0.036$) between nondiabetic and prediabetic CP patients, while sensitivity was 76.9% and specificity was 66.7% with AUC (71% and $p=0.008$) between prediabetic and diabetic CP patients. Comparison of ROC's between LysoPE and fasting blood sugar, with a sensitivity of 80% and 53%, specificity of 57% and 76% between nondiabetic and prediabetic patients and sensitivity of 77% and 53%, specificity of 67% and 76% between prediabetic and diabetic patients reveals LysoPE to be a better indicator for impaired glucose metabolism.

Conclusion: Our preliminary results suggest that phospholipid signature improves the detection of progression to diabetes in chronic pancreatitis.



* Role Of Genetic Evaluation In Children With Idiopathic Acute Recurrent Pancreatitis

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Introduction: Acute recurrent pancreatitis (ARP) is poorly understood in children. Several genetic risk factors have been identified in adults with ARP. However, literature regarding the genetics of ARP is sparse in the pediatric age group.

Aim: In this study, we aimed to analyze the genetic risk factors in children with ARP. **Methods:** All children (< 18 years) with ARP from Jan 2016 to May 2018 were prospectively enrolled in the study. Children with a known cause of ARP like obstructive, toxic/metabolic and autoimmune were excluded from the final analysis. Children with idiopathic ARP (IARP) underwent genetic testing for mutations/polymorphisms in genes known to predispose to ARP {SPINK1, PRSS1, CTSC (Chymotrypsin C), CTSB (Cathepsin B), CLDN-2 (Claudin-2) and CFTR}.

Results: A total of 239 children (116 boys, 10.3±3.7 years) were enrolled during the study period. Of these, 204 (85.35%) children were identified as IARP. The mean age of symptom onset and the average number of acute episodes were 8.3±3.7 years and 3.3 ± 1.8, respectively. In 4.6% (11/239) family history of pancreatitis was noted. Pancreas divisum was found in 18.7% (27/144) children. A genetic evaluation was performed in 144 (70.6%) children with IARP. Mutations/polymorphisms in at least 1 gene was identified in 89.5% (129/144) children including SPINK1 in 41.9%, PRSS1 (rs 10273639) in 58.2%, CTSC in 25.6%, CLDN-2 in 72.9% and CFTR in 2.3%. There was no significant in the incidence of genetic mutations/polymorphisms in IARP with or without pancreas divisum (95.7 vs 88.4%; p=0.467).

Conclusion: Genetic mutations are the most common cause of IARP in children. The incidence of genetic mutations is similar in children with or without pancreas divisum. The role of pancreas divisum in causing ARP in the absence of genetic mutations should be evaluated in future studies.

A Randomized Trial Of Short Versus Long Esophageal Myotomy During Per Oral Endoscopic Myotomy (Poem) In Management Of Achalasia Cardia (AC).

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Background: POEM is now established treatment for the management of Achalasia cardia. The technique of POEM is evolving and is yet not standardized. The primary aim of myotomy is to divide the muscular layer that constitutes the esophagogastric junction complex to reduce lower oesophageal sphincter pressure and relieve the obstruction. However, there is little evidence regarding the optimal length of this esophageal myotomy during POEM. This study was done to compare the outcomes of short (3 cm) versus long (6 cm and above) oesophageal myotomy in patients undergoing POEM for achalasia cardia.

Method: Fifty-six consecutive patients with AC (type 1 and II) undergoing POEM were randomized to receive short and long oesophageal myotomy. Operative details, the rate of adverse events, the symptoms and incidence of gastroesophageal reflux disease were compared in two groups. The data were collected prospectively and patients were followed for 6 months. During follow up patients were evaluated clinically, objective parameters including timed barium swallow study, OGD, and 24 hours pH metry were done and compared in two groups.

Results: Twenty-six patients received short and 30 patients received long esophageal myotomy during POEM. The baseline characteristics were comparable in both groups before the POEM. Mean length of esophageal myotomy in short and long group was 3.26 ± 0.6 and 11.03 ± 1.49 cm ($P=0.001$) respectively. The mean operative time was significantly shorter in short myotomy group (45.9 ± 16.9 and 72.2 ± 31.4 minutes, $P=0.001$). Clinical success was comparable in both the arms (Mean Post POEM Eckardt score of 0.38 ± 0.49 and 0.46 ± 0.51 , $P=0.38$). Manometric parameter (IRP of 9.53 ± 3.7 mmHg and 11.3 ± 6.72 mmHg, $P=0.23$), oesophageal emptying (post POEM barium column height of 3.5 ± 3.7 and 3.55 ± 3.23 cm, $p=0.9$) showed similar improvement in both the arms. Intraoperative complications and rate of gastroesophageal reflux (Acid exposure time, total reflux episodes and Deemsters score on 24 hours pH metry) were similar in both groups.

Conclusion: During the POEM procedure in the treatment of achalasia cardia (type I and II), short esophageal myotomy is associated with significantly shorter operative time with similar clinical success, adverse events, and reflux rates as compared to long esophageal myotomy.

Emerging IBD Demographics In South Asia And Middle East : A Pilot Study From The IBD Emerging Nations' Consortium (IBD-ENC)

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Background and Aims: Inflammatory bowel disease (IBD) is on the rise in the emerging nations of South Asia. The region is genetically distinct from Caucasian and Mongoloid populations. It shares a common geographic belt with similar socioeconomic conditions and challenges. Epidemiologic data is lacking from many of these countries. Phenotypic and demographic characteristics of IBD in this region have not been evaluated.

Methods: A retrospective study in 14 countries across South Asia and Gulf States (Afghanistan, Bangladesh, India, Indonesia, Kuwait, Malaysia, Myanmar, Nepal, Philippines, Qatar, Singapore, Sri Lanka, Thailand, UAE, Vietnam) used a standardized proforma comprising patient demographics, disease location, diagnostic delay, behaviour and treatment. Confirmed cases of IBD using standard criteria were enrolled. Cases were collated and analysed to identify trends in these nascent IBD countries. Patients with incomplete data were excluded. The data were compared to published data from the West and other Asian countries.

Results: We collected data on 10,380 patients. 320 were excluded due to incomplete data. 10059 patients (UC 6596, CD3213, IBDU250) were included in the analysis, with a UC:CD ratio of 2.05:1 (Table 1). 57.1% were male; median age of onset of UC was 32 years (SD 14.04, range 4-70) and for CD was 34 years (SD 14.00, range 4-76 yrs). Median diagnostic delay was 24 months (SD 3.05, range 1-40). Distribution of UC was 23% proctitis (E1), 47% left sided colitis (E2) and 30% pancolitis (E3). Distribution of CD was 32% ileal (L1), 38% colonic (L2), 24% ileo-colonic (L3) and 6% upper GI (L4). Behaviour of CD was inflammatory (B1, 63%), stricturing (B2, 20%), penetrating (B3, 10%). 7% had perianal disease (p). Extra-intestinal involvement was seen in 25% patients (15% peripheral joints 1% axial arthropathy, 8% skin or eye manifestations and 1% primary sclerosing cholangitis). Therapy for UC was 5-ASA (80%), corticosteroids (48%), immuno-modulators (IM, 27%) and biologics 4%. In CD, respective figures were 62%, 47%, 49% and 8%. 18% patients with CD had received empirical anti tuberculous therapy. Colectomy rate for UC was 0.5 % and bowel surgery in CD was 12%. Familial aggregation was noted in 4%. The proportion of smokers in UC and CD was 10% for both conditions.

Conclusions: UC was relatively more common than CD compared to the West, with a low colectomy rate, which may indicate milder disease. CD was predominantly inflammatory, with a lower rate of surgery than commonly reported in the West. Perianal disease was relatively uncommon and EIMs more common than reported from other Asian countries. Biologics were uncommonly used for treatment. IBD in the emerging nations of South Asia and Gulf States currently appears to have a distinct phenotype compared to more developed Asian countries and the West.

Table 1: Total number of IBD patients country wise and their subtypes: ulcerative colitis (UC), Crohn's disease (CD), Indeterminate colitis (IC)

COUNTRY	TOTAL No. of PATIENTS	UC	CD	IC	RATIO UC:CD
Afghanistan	28	21	7	0	3:1
Bangladesh	507	412	95	0	4.3:1
Egypt	74	37	37	0	1:1
India	6064	3788	2054	222	1.8:1
Kuwait	14	12	2	0	6:1
Indonesia	49	15	34	0	1:2.2
Malaysia	856	553	303	0	1.8:1
Myanmar	250	247	3	0	82.3:1
Nepal	118	75	38	5	1.9:1
Philippines	50	27	20	3	1.13:1
Qatar	526	399	127	0	3.14:1
Srilanka	703	454	229	20	1.9:1
Thailand	443	258	185	0	1.4:1
UAE	129	100	29	0	3.4:1
Vietnam	248	198	50	0	3.9:1
Total	10059	6596	3213	250	2.05:1

Novel Bio-Degradable Stent In Patients With Chronic Pancreatitis

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Introduction: Pancreatic stents are placed endoscopically for management of patients suffering from chronic pancreatitis. Currently used plastic pancreatic stents can occlude over a period due to the formation of biofilms leading to either recurrence of original symptoms or additional complications. Hence, a repeat ERCP procedure is required at later date after resolution of index event for stent removal or stent exchange to avoid adverse events. Biodegradable stents undergo gradual degradation over the variable period and may be considered to treat pancreatic ductal obstruction without the need for repeat endoscopic procedure for stent retrieval.

Aims and Methods: To assess the technical success and safety of ERCP guided placement of biodegradable stent (primary endpoint). For secondary endpoint, a self-assessment scale from 0 to 10 was used to assess the quality of life before and after stenting. Any adverse events were noted.

The pilot study enrolled subjects with symptomatic pancreatic duct obstructions requiring management by ERCP guided stenting. Biodegradable stents with three variable degradation profile were used. Serial abdominal X-rays were taken at 14 days, 1, 3, 6, 9, and 12 months after placement to monitor the position of the indwelling stent and its natural disintegration.

Results: 23 patients (17 males, mean age 38.4 years) were included with various indications (Table 1). Technical success was achieved in all subjects (n=23, 100%). There was no requirement of ERCP with re-stenting. There were no repeat ERCP for device retrieval in the study. The radiologic visualization of the biodegradable stent was rated as excellent (23%), good (64%) and fair (13%). There was one stent migration observed at day 30, without the need of any re-intervention up to 6 months follow up. (Table 2). The mean quality of life score showed improvement starting from 4.82±2.23 at baseline with rising to 7.47±1.49 at day 1 after index procedure with a further increase up to 8.13±1.54 at 30 days.

Conclusion: Biodegradable stents are safe for management of pancreatic duct obstruction in this pilot study and may be considered to avoid a second ERCP for stent removal. Further studies are needed to assess their more extensive use.

Indications for Biodegradable stent

Chronic pancreatitis (non-calcific)	6 (26%)
Chronic calcified pancreatitis + ESWL (recent)	8 (35%)
Chronic calcified pancreatitis + ESWL (past)	3 (13%)
Chronic calcified pancreatitis on stent exchange program	5 (22%)
Post-ERCP pancreatitis prophylaxis	1 (4%)

Predictors Of Hepatorenal Syndrome: Fractional Excretion Of Sodium Vs Fractional Excretion Of Urea

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Background: Acute kidney injury (AKI) in cirrhosis of liver (CLD) is associated with high short term mortality and Hepatorenal syndrome (HRS) is one of the major cause of AKI is associated with poor prognosis. Current diagnostic criteria diagnoses HRS retrospectively after 48 hours of admission and thus results in delayed definitive treatment initiation. FENa (Fractional Excretion of Sodium) and FEUr (Fractional excretion of Urea) are traditionally used to differentiate between prerenal AKI and intrinsic renal disease. We aim to ascertain their role in discriminating HRS and non-HRS acute kidney injury at admission.

Methods: In our prospective study, all inpatients more than 18yrs of age with CLD and AKI were included. Sodium, urea and creatinine were measured from both serum and urine samples. FENa and FEUr were calculated using standard formulas. Patients were treated as per standard protocol and were reassessed after 48hrs for the diagnosis of HRS and Non-HRS. Non-HRS were further divided into Pre-renal AKI and intrinsic renal disease. Patient with Chronic kidney disease, diuretic use less than 48hours and renal replacement therapy in the last 6 weeks were excluded from the study.

The statistical analysis include comparison of age, gender , survival status, FENa, FEUr between

3 groups and their comparison using ANOVA , students t test , and Fishers exact test. Receiver operating characteristic (ROC) was carried out between the 3 groups for FENa and FEUr to estimate sensitivity , specificity and other diagnostic parameters etc. SPSS and Med cal C softwares's were used.

Results: In our study, 113 consecutive chronic liver disease patients with acute kidney injury, admitted in critical and non-critical wards were enrolled. Majority of the patients were male (93.8%) with mean age of 48.8 (\pm 14.97) years & with ethanol (60.17%) as the most common etiology of CLD. In hospital mortality was higher in the HRS group than in the non-HRS group (26.2% vs 18.3%; p value: 0.348). The mean and Standard deviation of FENa and FEUr are as in table 1. A comparison between HRS and Non-HRS group (Fig 1) with a FENa cut-off 0.876% (AUC: 73.9%) showed a sensitivity of 100%, specificity of 47.8% (CI: 35.9% to 60.1%) and Negative predictive value 97.1% (CI: 85.1% to 99.3%). FENa was lower among HRS group than in Pre-renal AKI group in comparison, but was not statistically significant (P value: 0.674). FEUr did not differentiate HRS neither with non-HRS group (P value: 0.345) nor with Pre-renal AKI group (P value: 0.659).

Conclusion: It is probably the first prospective study comparing FENa and FEUr among CLD patients with AKI. FENa is better predictor of HRS and Non HRS with high negative predictive value, than FEUr among CLD patients with AKI.

	FENa		FEUr	
	Mean	SD	Mean	SD
HRS (42)	0.365	0.215	0.457	0.784
Pre renal AKI (39)	0.437	0.334	0.320	0.279
Intrinsic renal disease (32)	2.764	1.81	0.856	1.54
P value (ANOVA)	0.001		0.06	

Table: 1

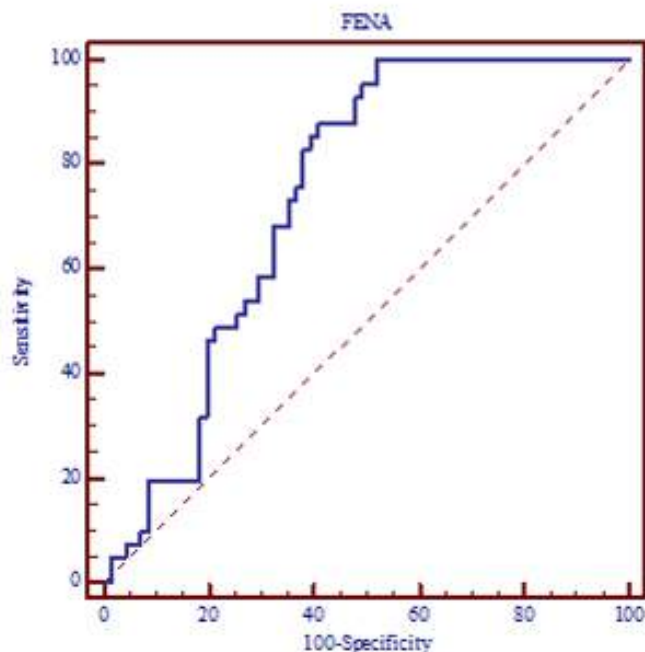


Fig 1

Randomized Sham Controlled Trial Of Endoscopic Full Thickness Plication For The Treatment Of PPI Dependant Gerd

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Introduction: GERD-X, an endoscopic full thickness plication device, is a novel minimally invasive endoscopic device for the treatment of patients with chronic GERD. With this endoscopic device, transmural sutures are applied at the gastroesophageal junction (GEJ), leading to the reconstruction of the gastric cardia and thereby accentuating the valvular mechanism to prevent reflux. In this RCT, we evaluated the (1) technical success (2) safety and efficacy of GERD-X over the short term period for management of patients with chronic GERD well controlled on PPI therapy.

Methods: Patients with symptomatic GERD on PPI therapy for at least 6 months and documented pathological reflux on 24-h pH impedance monitoring were randomized to GERD-X versus a sham procedure in a ratio of 1:1. Technical success was defined as the successful application of at least 2 transmural sutures at the GEJ. Clinical success was defined as an improvement in the GERD-HRQL total score by >50% at 3 months. Complications in both groups were noted. At 3 months, outcomes were compared between the treatment and sham group using Mann Whitney U test.

Results: 67 patients with prospectively enrolled in this RCT. Baseline characteristics of GERD-X (n=37) and Sham (n=30) groups were comparable. Technical success was achieved in all patients (100%) in the GERD-X group. At 3 months, the proportion of patients achieving clinical success i.e. >50% improvement in GERD-HRQL total score was significantly higher in the GERD-X group compared to the sham group [58% vs. 30%; p=0.021]. In addition, there was a significant reduction in GERD-HRQL heartburn score at 3 months from baseline in GERD-X [14(10-21) vs. 5 (0-12); p=<0.001] compared to sham [8 (0-50) vs. 5.2 (0-11); p=0.931]. Mild chest pain and self-limiting pleuritis were reported in 2 patients after GERD-X. At 3 months, 40% of patients in the treatment group vs 27% of patients in the sham group were off PPI therapy.

Conclusion: Results from this prospective randomized controlled trial show that Endoscopic full thickness plication is a safe and efficacious technique. There is a significant improvement in the GERD symptoms and health related quality of life over short term follow up. Long term results are awaited.

