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9TH EURO GLOBAL GASTROENTEROLOGY CONFERENCE

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Interleukin-1 receptor antagonist knockout mice as a model of the inflammatory bowel disease

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The inflammatory cytokine Interleukin 1 (IL-1) is an important mediator of inflammation and tissue damage in inflammatory bowel disease (IBD). The activity of IL-1 is inhibited by a natural inhibitor; interleukin 1 receptor antagonist (IL-1Ra). The balance between IL-1 and IL-1Ra plays a vital role in diseases. We investigated whether inflammatory bowel disease could be induced spontaneously by the removal of IL-1Ra in mice. Histological staining was performed on BALB/C mice to characterize the morphology and enzyme activity of the small intestine from different ages and genotypes. Wild type mice served as a negative control. 20 well oriented villi/crypt units and villus width at midvillus in longitudinal tissue sections were measured in the jejunum and ileum. The number of goblet cells per villi was determined. Immuno histochemical staining was performed to localise and detect MUC2, MUC5AC, MMP2, MMP9, ADAMTS1, IL-1 β and TNF α . The results showed that there was a significant decrease in the villi/crypts units' height in the jejunum and ileum whereas the width of the villi was increased in the jejunum and decreased in the ileum. The number of goblet cells per villi was increased in knockout mice compared with wild type mice. Research is ongoing for the analysis of the immunohistochemistry. We conclude that IL-1Ra knockout mice could act as a model for inflammatory bowel disease highlighting the importance of IL-1 in this disorder.

Biography

Rasha Hatem Saeed Dosh has completed her MSc from Al-Mustansiriyah University and worked as a Lecturer at University of Kufa College of Medicine/Iraq. She has published 4 papers in college of medicine journals. She is currently a second year PhD student at Sheffield Hallam University/UK.

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Comparison of safety according to the timing of flumazenil administration in sedative endoscopy with midazolam: A single center, prospective, randomized and double-blinded study

Hong Soon Jung

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Flumazenil is a benzodiazepine antagonist that blocks the central effects of benzodiazepines. Previous studies suggest that routine use of flumazenil after midazolam sedation for endoscopy shorten the recovery time, but there is no data on timing of flumazenil administration. In this study we assessed the timing of flumazenil in outpatients receiving intravenous sedation with midazolam. From 2012 August to 2015 July, 74 participants undergoing sedative diagnostic endoscopy with midazolam were prospectively included. They were randomized in a double-blind to receive either flumazenil immediately (immediately group) or 30 minutes later after the procedure (delayed group). Four hours after the sedative endoscopy each patient was interviewed by telephone to assess the primary end point, sleepiness and dizziness. 74 participants were analyzed, 37 with immediate administration of flumazenil and 37 with delayed administration. There were no significant differences between the two groups in age, sex, blood pressure, pulse rate, the average dose of midazolam, procedure duration, recovery time, previous history of endoscopy and satisfaction score from the patients. Also, there was no significant difference in sleepiness and dizziness between immediately group and delayed group. Sleepiness (immediately injected group=56.8%, delayed injected group=45.9%) and dizziness (immediately injected group=24.3% and delayed injected group=40.5%) was observed in almost half of the participants, in particular within two hours. In this prospective, randomized, double-blinded clinical trial showed that there is no significant difference in safety between two groups. Patient who received flumazenil should be monitored for 2 hours after its administration because of the potential for re-sedation.

Biography

Hong Soon Jung has completed his MD from Catholic University of Korea and Post-doctoral studies from Catholic University Korea, College of Medicine. He is now working in the Division of Gastroenterology of Seoul St. Mary's Hospital and Fellowship training.

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Multidisciplinary approach to the treatment of chronic pancreatitis in children – Institutional experience

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Chronic Pancreatitis is a chronic inflammatory disease characterized by fibrosis and destruction of exocrine pancreatic tissue. It is prevalent in many parts of the world with varying epidemiological profiles in different areas. There is a relatively high prevalence of such disorders in southern India. In most series, the etiologies are trauma, biliary tract distension are unknown. In majority of CP in children, medical therapy alone suffices and surgical intervention is reserved for complications. This study was conducted to establish the clinical profile of pancreatic disorders in pediatric patients ranging in age from 1 to 19 years in a tertiary care hospital in southern India. The records of the patients up to 19 years of age diagnosed to have pancreatitis at our institution for the last 12 years were reviewed with a proforma to record the following parameters: Age, gender, presenting complaints, examination findings, investigations, management with medical treatment, surgical intervention or both and complications. There were 50 patients ranging from age group 3 to 19 years, out of which 30 were males and 20 were females. 41 patients were between the ages of 11-19 years, 5 were between the age of 6-10 years, and 4 were between the ages of 1-5 years. 28 patients presented with acute on chronic pancreatitis and 22 patients had calcific chronic pancreatitis. The etiology of CP in 42 patients was idiopathic, in 4 was biliary tract disease, 2 were alcoholic, and 2 were congenital (pancreatic divisum). Complications like pseudo cyst was seen in 19 patients, ascites in 4, diabetes in 3, pleural effusion in 3, splenic thrombosis in one, acute necrotizing pancreatitis in one, retroperitoneal abscess in one and acute renal failure in one patient. Apart from medical line of management, 12 patients underwent stenting of pancreatic duct and 10 underwent surgical treatment for complications. Among the complications, acute relapses of chronic pancreatitis were the most common. 38% of the patients had pseudocysts, 44% had calcific pancreatitis, 6% developed diabetes, 8% had ascites, 6% had pleural effusion and there were 3 deaths due to sepsis.

Biography

Vijay Kumar is a Professor and Head of Dept. of Pediatric Surgery in Kasturba Medical College, Manipal University . He had 41 scientific articles in various international and national journals. He presented 12 scientific papers at various international conferences held at Bangkok, Malaysia, Sri Lanka, Nepal, Dubai, UK, USA, etc. He presented more than 60 scientific papers at various national conferences, workshops held in different parts of India. He gave more than 30 scientific deliberations at various national, international conferences, workshops, scientific congresses, medical associations and chapters. He attended 15 pediatric surgery and pediatric urology workshops at national and international level as a resource person. He is an active member and office bearer in many social organizations. He organized and participated in many free medical camps in the community. He gave many talks on health awareness in the Radio and TV shows.

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Serum levels of ADAM 12 and ADAM 17 in patient with colorectal cancer depending on the staging and grading

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ADAM proteins belong to the family of matrix metalloproteinase. In humans identified ca. 20 members of this group. The main role of these proteins are involved in the processes of migration, adhesion and cell proliferation, hence their importance in the process of carcinogenesis. In the present study, we examined the relationship between serum levels of ADAM 12 ADAM 17 in patients with colorectal cancer depending on the staging and grading. The study included 70 patients (41 men, 39 women), age: 32-88 years (mean age 69.01). Protein concentrations in serum were determined by ELISA and the results are compiled in the Statistica 12. ADAM 12 protein concentrations ranged 0, 6-26, 72 ng/ml (mean: 5.00 ng/ml). Protein concentrations of ADAM 17: 0, 44-9, 83 ng/ml (mean: 2.09 ng / ml). In the study group, 31 patients were classified as early stage of the disease (TNM I-IIc). In the study group dominated second degree of histological malignancy (G2 - 48 patients) and the most common type of cancer was *Adeno carcinoma*. Based on the analysis, there was no significant relationship between the degree of clinical stage and histological grade of colorectal cancer and serum concentrations of ADAM 12 and 17. Moreover positive relationship between serum concentration of ADAM 12 and ADAM 17 was found. In our view, research on the role of ADAM proteins in colorectal cancer need to be continued, and presented results can be a starting point for further projects.

Biography

Paweł Kozieł has graduated from Silesian Medical University in 2011 and he works in Department of Internal Medicine in Bytom as Junior Assistant. Currently, he is also a PhD student in the Medical Doctor program at Silesian Medical University in Katowice. His works were recently published in 4 international journals and 2 local journals, in the areas of gastroenterology, oncology and endoscopic techniques in particular.

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The profile of melatonin receptors gene expressions and genes associated with their activity in colorectal cancer patients

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The antiproliferative and immunomodulatory effects of melatonin (MLT) have been demonstrated in a variety of neoplasms including colorectal cancer (CRC). In humans and other mammals, MLT acts on target tissues through membrane and retinoid nuclear receptors. The aim of the study was to evaluate transcription activity of melatonin receptors and genes associated with regulation of their activity in colorectal adenocarcinoma tissues in relation to clinical stage of cancer. A total of 24 pairs of surgically removed tumoral and healthy (marginal) tissues samples from colorectal cancer patients at clinical stages I-II and III-IV were collected. As the additional control, twenty normal samples were taken from people whose large intestine tissues were reported as non-tumoral after colonoscopy. Expression of mRNA genes was studied by microarray HG-U133A analysis. The analysis of genes expression profile was performed using commercially available oligonucleotide microarrays of HG-U133A (Affymetrix, Santa Clara, CA). We found a high increase of MT1 mRNA expression levels in all cancerous samples vs. non-cancerous tissues. The MT2 mRNA expression levels increased slightly in marginal and malignant samples. The melatonin receptors gene expression was dependent on tumour grade. Among the genes participating in the cascade of signal transfer in cell activated by MLT via MLT1 and MLT2, the following ones: GNA11, OXTR, and TPH1 encoding genes respectively as differentiating stage III and IV of CRC. Monitoring the expression levels of genes that are related to melatonin receptors may offer a strategy to anticipate tumour development and estimate the molecular changes that occur during carcinogenesis. The mechanism behind this association needs further elucidation.

Biography

P Kozieł has graduated from Silesian Medical University in 2011 and works in Department of Internal Medicine in Bytom as Junior Assistant. Currently, he is also a PhD student in the Medical Doctor program at Silesian Medical University in Katowice. His works were recently published in 4 international journals and 2 local journals, in the areas of gastroenterology, oncology and endoscopic techniques in particular.

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Pentasa enema in acute pancreatitis patients: A case report

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The amino salicylates have a direct local anti-inflammatory effect on the mucous membrane of the small intestine and colon. They have been used for many years in the treatment of inflammatory bowel disease (IBD), these are, generally, well tolerated, however, like all drugs; they may, in rare cases, cause side effects. We report a patient with a distal ulcerative colitis who presented with acute pancreatitis under Pentasa® enema.

Observation: This is a patient of 24 years old, without medical history, followed for a year due to a distal ulcerative colitis. Initially he was treated by oral corticosteroids (Cortancyl 60 mg); the steroid dose was tapered to 20 mg with recurrence of clinical manifestations (diarrhea 08 stools/day+rectal urgency), rectosigmoidoscopy indicates exacerbation of his illness. The decision was to put the patient on a dose of 60 mg Cortancyl associated with a local treatment with Pentasa enema to reduce the rectal syndrome. The patient presented 03 days after a violent epigastric pain radiating to the back associated with bilious vomiting, with laboratory showed a lipase 7x normal. The diagnosis of acute pancreatitis was retained with an abdominal CT scan after 48 hours that showed a normal sized homogeneous pancreas, (stage A of Balthazar), normal pancreas, acalculous gallbladder, and no intra or extra hepatic bile duct dilatation. The calcium and triglyceride were normal, IgG4 was also normal. The patient was strictly fasted for 48 hours and the Pentasa® enema suspended.

Evolution: The evolution was marked by the disappearance of pain and vomiting with normalization of lipase and enteral nutrition was retained without any difficulties. The diagnosis is pancreatitis in 5-ASA.

Conclusion: The acute pancreatitis secondary to amino salicylates is a very rare complication. In our case, taking the Pentasa® enema for 03 days was sufficient to cause acute inflammation of the pancreas.

Biography

Khalid Abdelwali completed his MBChB in 2005 from Faculty of Medicine, Assuit University and then worked in Assuit University Hospital for 1 year. After that, he started working in Manshyet Elbakry Hospital in Cairo, Egypt in the Department of Gastroenterology and Liver Diseases, and then a part time Physiology Lecturer in Misr International University. He finished his Diploma in Internal Medicine in 2014 at Ain Shams University, Egypt. He then moved to the Department of Gastroenterology and Liver Diseases in Sheikh Zayed Al Nahyan General and Specialized Hospital, Cairo. He is a resident in the Department of Gastroenterology and Liver Diseases, Ibn Sina University Hospital, Rabat, Morocco.

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Hepatitis B Virus envelope variability of genotype A strains correlated with HBsAg persistence in patients with acute or chronic hepatitis B and in HBV/HIV co-infected patients.

ESCHLIMANN Marine

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Around 240 million people are chronically infected by Hepatitis B virus (HBV) worldwide. The clearance of HBV surface Antigen (HBsAg) correlated with a good clinical prognosis is rarely achieved, even on anti-HBV treatments. HBV envelope proteins play a crucial role in virus cellular entry and in immune recognition. Our hypothesis is that the variability of HBV envelope proteins could influence HBsAg clearance or persistence, as suggested in our previous study on HBV genotype D (Velay et al., JVH, 2016). This study was extended to HBV genotype A infected patients with different clinical profiles: acute (n=4) or chronic hepatitis B (n=6) and HBV/HIV coinfection under treatment (n=6). In each group, patients with HBsAg clearance (Resolvers-R) were compared to Non-Resolvers (NR). For this purpose, HBV S and preS sequences were studied by bulk genotyping and ultra-deep sequencing (UDS). Amino acid sequences were analyzed with bioinformatics for predicted antigenicity. More frequent major mutations were observed in S gene than in preS region (p=0.02 in acute HBV infection). Among mutations found exclusively in NR, nine were observed several times (W4stop, T173K/A in preS; R79H, T118A, F134Y, Y161F, E164D, V209L in S). The mutation sY161F, found in four NR, led to a decrease in predicted antigenicity (22.6%). In the pol gene overlapping the S gene, the number of mutations tended to be higher in treated than in untreated patients (7.7 vs 3 mutations/patient). These results argue in favor of an influence of HBV envelope variability on the evolution of Hepatitis B in various clinical contexts.

Biography

Marine ESCHLIMANN is a PhD student, currently the second year of her thesis. After a license in Cell Biology and Animal Physiology at the Faculty of Sciences, Reims, France, she focused on Microbiology in the Master BioMANE at the Faculty of Sciences, Nancy, France. After a study on bacterial biofilms, she was involved in a research program in Virology, in the University of Medicine, Nancy, France, with Pr E. Schvoerer *et al.* Thus she contributed to several investigations on the variability of HBV envelope proteins with the support of a ministerial scholarship.

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Tobacco expression of novel envelope proteins-derived HBV antigens for cost-effective vaccine development

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Hepatitis B virus (HBV) infection represents a serious public health problem especially in developing countries. Despite the availability of a safe and efficient commercial vaccine, its use in mass immunization programs is hampered because of the high costs. Moreover, 10% of the vaccinated population develops a low immune response. In this context, we aim to design new HBV antigens in order to develop a more immunogenic vaccine in plants, as a low-cost alternative. Our strategy is focused on the antigenic properties of the large (L) envelope protein and on the ability of the small (S) surface antigen (HBsAg) to self-assemble into subviral particles (SVPs). HBsAg was used as a carrier for the 21-47 L-derived peptide by insertion in the antigenic loop (AGL) of HBsAg and by replacing a fragment from the AGL. The chimeric proteins along with the wild-type S protein were produced in green plants (*Nicotiana benthamiana*) and in HEK293T cells, as a reference system. Expression of the antigens was investigated in both production systems and properties like protein folding, dimerization and N-glycosylation were analyzed. The immunogenic properties of the newly produced antigens are currently investigated. To conclude, the new antigens represent promising candidates for the development of new vaccines against HBV.

Biography

Mihaela-Olivia Dobrica was graduated in Biochemistry from University of Bucharest, Romania in 2012 and completed her Master's degree in Neurobiology from University of Bucharest, Romania in 2014. She is currently pursuing PhD at the Institute of Biochemistry of the Romanian Academy, Department of Viral Glycoproteins.

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Crohn's disease and intestinal tuberculosis, two overlapping conditions

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Introduction: Differentiating intestinal tuberculosis from Crohn's disease (CD) is a clinical challenge of therapeutic significance, because tuberculosis is mimicker to CD as regard symptomatology, clinical and radiological examination.

Case Description: Here, we report a case of chronic progressive constipation and abdominal distention due to intestinal tuberculosis that was previously mistreated as Crohn's disease. Surgery with resection anastomosis of the small bowel stricture was performed, followed by 6-month standard treatment for miliary tuberculosis, which was diagnosed on the basis of the presence of acid-fast bacilli in the diseased bowel and positive culture of *M. tuberculosis* from ascites, and stool samples. The patient was examined for 6 months after and well recovered thereafter.

Conclusion: The final diagnosis of intestinal tuberculosis can sometimes be confirmed by operation room biopsies, rescue the patient from abdominal emergency, and provide a chance for cure.

Case report: A 45-year-old man experienced recurrent abdominal pain, constipation and weight loss (12 kg) in 1 year. He was diagnosed as CD on the basis of abdominal CT scan, and colonoscopic findings. CT abdomen showed skip lesions throughout the small bowel. Colonoscopic examination showed the presence of multiple terminal ileac polypoid formations of which multiple biopsies were taken. The pathologic report was chronic inflammatory changes. Treatment of CD, prednisolone and azathioprine were then prescribed with a poor response. He presented to emergency room with diffuse abdominal pain fever and absolute constipation after treatment for CD. CT scan of the abdomen revealed intestinal obstruction due to the old iliac stricture. Emergent laparotomy with segmental small bowel resection was performed. The pathologic report showed granulomatous inflammation with the presence of acid-fast bacilli. Miliary TB was diagnosed with additional positive findings of polymerase chain reaction (PCR) and positive culture for *M. tuberculosis* in sputum, stool, and ascites.

Discussion: ITB accounts for 1–3% of all TB cases. Differentiating between ITB and CD, especially in areas endemic for TB, is quite challenging since both can present as granulomatous inflammation. CD is characterized by a progressive transmural inflammation with skip lesions throughout the GI tract. Although many presentations of ITB and CD are similar, certain clinical and histological features can be helpful in distinguishing between them. The presence of ascites is usually an indication of ITB rather than CD because peritoneal involvement is uncommon in the CD. Endoscopic biopsies should be done if feasible. Combination of endoscopic and histological features could increase the diagnostic rate to around 60%.

Conclusion: The similarity between CD and ITB should be kept in mind whenever possible, especially in areas endemic for TB as mistreatment prolongs the ITB course and even lead to complications. The combination of serial biopsies/ surgical pathology and endoscopic features is mandatory in increasing diagnostic accuracy.

Biography

Khalid Abdelwali completed his MBCh in 2005 from Faculty of Medicine, Assuit University and then worked in Assuit University Hospital for 1 year. After that, he started working in Manshyet Elbakry Hospital in Cairo, Egypt in the Department of Gastroenterology and Liver Diseases, and then a part time Physiology Lecturer in Misr International University. He finished his Diploma in Internal Medicine in 2014 at Ain Shams University, Egypt. He then moved to the Department of Gastroenterology and Liver Diseases in Sheikh Zayed Al Nahyan General and Specialized Hospital, Cairo. He is a resident in the Department of Gastroenterology and Liver Diseases, Ibn Sina University Hospital, Rabat, Morocco.

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Activation of Macrophage and Its Impact on structural defects of rat Liver in experimental Diabetes

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Statement of the Problem: The Morphofunctional state of the liver in diabetes mellitus should be assessed since all metabolic processes occur in liver; hepatocytes have the insulin-dependent mechanism of glucose metabolism and 40-60% of insulin is inactivated in liver. The structure of damaged liver tissue and mechanisms of hyperglycemia which cause the damage were described in many investigations. The assessment of various methods of damaged liver correction was performed. It is known that hepatic macrophages play key role in tissue injury and repair. However, its effects on regenerative processes in diabetic liver are not investigated enough. We previously set that the macrophage modulator 3-aminophthalhydrazid (3-APH) activated anti-inflammatory and antioxidant functions in monocyte-macrophage cells.

The purpose of this study: is to evaluate the impact of macrophages activated by 3-APH on structural defects in diabetic rat liver.

Methodology: A damaged liver tissue and hepatocyte reparation were studied in alloxan diabetic rats after modulation of macrophage activity by 3-APH during 30 and 60 days.

Finding: The morphological study of diabetic liver tissue revealed degenerative changes in hepatocytes, inflammatory processes in the portal and intralobular stroma, microangiopathy and blood circulation disorders. Structural disorders of liver parenchyma increased at a prolongation of AD up to 60 days. It was found that the administration of 3-APH contributed to reduction of damage and restoration of normal liver histological structure due to activation of reparative processes.

Conclusion: Thus, macrophage activation in diabetic liver causes increase in hepatocyte activity and compensation of structural damage in liver tissue. 3-APH is likely to be a promising drug for correction of liver tissue in diabetes due to its hepato protective effect.

The study is supported by the grant from the Russian Science Foundation, the project № 16-15-00039.

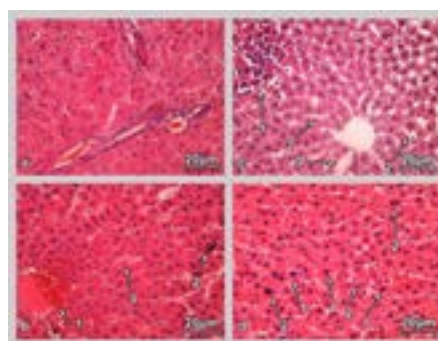


Figure 1: a - histological structure of intact rat liver tissue. b –diabetic liver tissue (30 days): 1- plethora in central venules, 2- lymphocytic infiltration of sinusoidal capillary, 3 - degeneration of hepatocytes. c – diabetic liver tissue (60 days): 1 - intralobular necrosis of hepatocytes, 2 - edema, vasodilatation, 3 - desquamation of endothelial of sinusoidal capillaries. d –diabetic liver tissue (60 days) treated by 3-APH: 1 - polyploid hepatocytes, 2 – dual-nucleus hepatocytes. Staining by hematoxylin-eosin. X400

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Recent Publications

- Lucchesi A.N. et al. (2013) Diabetes mellitus triggers oxidative stress in the liver of alloxan-treated rats: a mechanism for diabetic chronic liver disease. *Acta Cirurgica Brasileira* 28.7: 502-508.
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- Holt M.P., Cheng L., Ju C. (2008) Identification and characterization of infiltrating macrophages in acetaminophen-induced liver injury. *Journal of leukocyte biology* 84.6: 1410-1421.
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- Welt K. et al. (2004) Ultrastructural, immunohistochemical and biochemical investigations of the rat liver exposed to experimental diabetes und acute hypoxia with and without application of Ginkgo extract. *Experimental and Toxicologic Pathology* 55.5: 331-345.

Biography

Irina Danilova, professor, director of the Fundamental Medicine department of the Ural Federal University (UFU), Yekaterinburg, Russia. She is an author of more than 220 scientific publications, "Macrophages Non-immunological Functions" monograph and 5 patents including an EU, USA patent. Irina Gette is a scientific associate of UFU, PhD. She has published 97 papers in reputed journals. Musa Abidov a professor, he is a creator of 3-aminophthalhydrazid. The scope of their research interests has impact on investigation of macrophages during reparative processes in tissue under various pathological states.

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Bacterial epidemiology and antimicrobial resistance in ascitic fluid in cirrhotic patients between 1988 and 2016 at the University Hospital of Brest (France)

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Background and aims: Spontaneous bacterial peritonitis (SBP) is the most typical infection and a common complication in cirrhotic patients with ascites. SBP has a poor prognosis with a one-year survival rate from 30 to 50% after the first episode, and an in hospital mortality below 30%. Recent studies showed the emergence of resistant bacteria leading the failure of first line antibiotic therapy. The aims of the present study were: a) to describe bacterial epidemiology and antimicrobial resistance in ascitic fluid in cirrhotic patients over time between 1988 and 2016, b) to evaluate their impact on 30-day mortality.

Methods: We conducted a retrospective study including 152 cirrhotic patients with SBP diagnosed on cytological criteria, between 1988 and 2016 in our center. Multivariate logistic regression was used to study predictors of 30-day mortality on overall population and from 1988 to 1999 vs 2000 to 2016.

Results: The mean age of patients was 60.1 years and 81% of patients were male. 80.1% of patients were C of Child-Pugh classification. The distribution of the isolates was the following: 44.4% Gram-negative with predominance of *Escherichia Coli* (n=51) 22.5% Gram-positive bacteria with predominance of *Streptococcus* (n=24), with no significant differences between the two periods. Regarding bacterial resistance, there were 0.7% (n=1) multi resistant bacteria (ESL producing *E coli*), 17.9% of quinolones resistant bacteria, 4.6% of third generation cephalosporines resistant bacteria, and 11.8% of amoxicillin-clavulanate-resistant bacteria, with no significant differences between the two periods. Eight percent of patients received prophylaxis, primarily norfloxacin. Acute kidney injury was the major predictor of 30-day mortality in overall population and considering each period. We also found that low blood pressure at admission, gastrointestinal bleeding, prothrombin time and Child-Pugh C score were independent risks factors of short term mortality. There was no impact of epidemiological changings or resistance on 30-day mortality.

Conclusion: Our study show relative epidemiological changes in bacteria isolated SBP in our center over a 28-year period, however a relatively low proportion of multi resistant bacteria as compared with results from other centers in France and in Europe. Our results confirm the prognostic role of acute kidney injury during SBP episodes and the beneficial effect of albumin infusion. We failed to show an impact of epidemiological changings or resistances on mortality but preventing measures should be applied as suggested in recent studies with higher resistances rate.

Biography:

Bertrand is a Member of the French National Society of Gastroenterology, Member of the French Society of Digestive Endoscopy, and Former Member of the American Gastroenterological Association. He is well experienced as a Doctor in Hepato-gastroenterology Center Brest 1989 - Present (27 years). He is a Former intern in Hospitals, Former head of clinic Universities, Practitioner Consultant in CHU Brest, Gastroenterology, Digestive interventional endoscopy, Hepatology, Endoscopy Bilio-pancreatic Digestive cancer, Nutrition, Medical and surgical proctology, Training.

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Higher efficacy of sequential therapy with pegylated interferon-alpha 2b and tenofovir compared to tenofovir monotherapy in HBeAg positive chronic hepatitis B patients

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Introduction: Monotherapy with PEG-interferon (PEG-IFN- α) or nucleotide analogues (NA) are largely ineffective in chronic hepatitis B (CHB) patients. A sequential combination therapy may have better therapeutic effects by sustained viral suppression combined with immunomodulation.

Aim: To Study the high efficacy of sequential therapy with pegylated interferon-alpha 2b and tenofovir compared to tenofovir monotherapy in HBeAg positive chronic hepatitis B patients.

Methods: One hundred twenty six treated naive HBeAg (+) CHB patients with moderately elevated alanine aminotransferase (ALT) (48-200 IU/mL) received tenofovir 300 mg/day for 72 weeks with PEG-IFN-a2b 1.5 mcg/kg per week added after first 12 weeks (lead-in-period) for 24 weeks (sequential combination therapy; ST) or tenofovir monotherapy; 300 mg/day for 72 weeks (TM). Primary end point was rate of HBeAg loss. Biochemical and virological responses were assessed at weeks 12, 36, 48 and 72 weeks. Combined virological response (CVR) [HBeAg loss and HBV DNA<2000 IU/ml at week 72] was also determined.

Results: At week 72, HBeAg loss occurred in 35.8% in ST group and 17% in TM group ($P=0.028$; OR: 2.73, 95% CI: 1.09 to 6.79). Combined virological response (CVR) was seen in 20.8% and 11.3% ($P<0.05$), respectively. No patients on ST group had HBeAg seroreversion at last follow up. At week 72, undetectable HBV DNA was seen in 77.4% (ST group) vs. 71.7% (TM group); ($p=0.51$) and normal ALT was seen in 62.3% and 52.8% ($p=0.32$), respectively. Significantly more patients on ST group had >3Log HBV DNA reduction at week 36 (92.5%) compared to TM group (66%) ($P=0.001$). Four (7.5%) patients on ST achieved HBsAg loss compared with MT (1 patient, 1.8%) by week 72. No patient had treatment related major adverse effect requiring discontinuation of therapy.

Conclusion: 24 weeks of PEG-IFNa2b as add-on sequential regimen to TDF is safe and resulted in more HBeAg and HBsAg loss, when compared to TDF monotherapy in selected HBeAg (+) chronic hepatitis B patients. Long-term follow-up trials are needed to assess for sustained durable response.

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Restaging rectal cancer after neoadjuvant chemo radiotherapy: For a down-staging classification

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Today neoadjuvant chemoradiation for T2 and T3 rectal cancers is widely adopted. Surgery is usually performed after 5-6 weeks from the beginning of the therapy and it is our policy to perform a restaging of the tumor at that moment, in order to obtain its down-staging, to discover possible complications related to the treatment, to confirm or adjust a surgical strategy, to evaluate risks for possible recurrence, and to schedule an adequate follow-up. For this, we have implemented a classification of the tumor down-staging, mainly based on radiological imaging results, contrast-enhanced computed tomography and magnetic resonance, and inspired to the current TNM scheme. Neoplastic regression inside rectal walls and mesorectum have been considered of prominent significance, and, therefore, discriminating in surgery. Besides, these aspects correlate well with the biological attitude of rectal cancer to regress following a centripetal way, starting from the most peripheral and recent zones of infiltration toward the central core of the tumor, where the tissue involvement is more marked. Interestingly, in our experience of 38 cases observed in the years 2012-2015, the down-staging score appears inversely correlated with the histological grading of the tumor, but directly with the Dowrak's tumour regression. Certainly our classification needs to be confirmed by further clinical studies, which will have to consider also the different molecular characteristics of rectal cancer.

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9TH EURO GLOBAL GASTROENTEROLOGY CONFERENCE

October 24-25, 2016 Valencia, Spain

Aurora kinase A is a prognostic marker in colorectal cancer patients

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Background & Aim: Aurora kinase A is a member of the serine/threonine kinase family and plays important roles in mitosis and chromosome stability. This study aimed to evaluate the clinical significance of Aurora kinase A expression in colorectal cancer patients in Korea.

Methods: Aurora kinase A protein expression was evaluated by immunohistochemistry in 151 patients with colorectal adenocarcinoma using tissue microarray blocks. We then analyzed the relationship between clinicopathological characteristics and Aurora kinase A expression. In addition, we assessed the prognostic significance of various clinicopathological data for progression-free survival.

Results: Aurora kinase A expression was detected in 45% (68/151) of the cases. Positive staining for Aurora kinase A was observed more often in male patients ($P=0.035$) and distally located tumors ($P=0.021$) progression-free survival was shorter in patients with Aurora kinase A expression compared to those with low-level Aurora kinase A expression ($P<0.001$). Univariate analysis revealed that Aurora kinase A expression ($P=0.001$), age ($P=0.034$), lymphatic invasion ($P=0.001$), perineural invasion ($P=0.002$), and TNM stage ($P=0.013$) significantly affected progression-free survival. In a multivariate analysis of progression-free survival, a Cox proportional hazard model confirmed that Aurora kinase A expression was an independent and significant prognostic factor in colorectal adenocarcinoma (hazard ratio, 3.944; $P<0.001$).

Conclusions: Thus, Aurora kinase A could serve as an independent factor to predict a poor prognosis in Korean colorectal cancer patients.

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Endoscopic and morphological features of gastroduodenal pathology in adolescents with connective tissue disorders

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The aim of the present study is improving prophylaxis and treatment of chronic gastroduodenal pathology in adolescents on the basis of determining clinical, endoscopic, and morphological peculiarities of said pathology. A total of 155 adolescents 11 to 18 years of age with inflammatory-destructive diseases of the upper gastrointestinal tract and Connective Tissue Disorders (CTD) were studied. The traits of the CTD, including the Marfan syndrom, were determined relying on the Ghent criteria. Morphological peculiarities are represented by high frequency of reflux-gastritis (77%) and a reduction in the level of interstitial collagens type 3 and type 1 in the lamina propria of gastric and duodenal mucosa. The form of mucosal lesions is a chronic non-atrophic (surface) gastritis with simultaneous inflammation in the antral and fundal parts. Duodenal ulcer was detected in 12% only and it was accompanied by detection of *Helicobacter pylori*. The connective tissue matrix of the mucosa is characterized by structural transformation of collagen fibrils (wrong orientation, focal sclerosis, immaturity). It is accompanied by decrease in a mucosa functional ability with development of the valve-sphincter failure. The role of CTD in the development of gastroduodenal pathology in puberty has been established. A genetically dependent insufficiency of interstitial collagens is a major cause of development bile reflux, which is a leading factor of gastroduodenal pathology formation in adolescents with CTD. The work provides grounds for employing in adolescents with CTD rehabilitation measures, connected with a prevention of reflux-gastritis progression and stimulation of the collagen synthesis.

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9TH EURO GLOBAL GASTROENTEROLOGY CONFERENCE

October 24-25, 2016 Valencia, Spain

MicroRNA expression varies depending on the site of inflammation during ulcerative colitis

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Ulcerative colitis (UC) is a type of inflammatory bowel disease, considered as an important disease of gastrointestinal tract having a huge impact on the health of the patient. The current study was performed to dissect out the site specific miRNA expression in the colon biopsy samples of UC patients from Northern India. Biopsy samples were collected from UC patients and healthy controls from Rectosigmoid area (RS) and Ascending Colon (AC). MicroRNA expression was compared between patients with RS and AC using a microarray platform. Differential expression was further validated by Real Time PCR analysis. Upon analysis of data generated on a microarray platform and qRT PCR revealed that the expression of six miRNAs hsa-miR-146b-5p, hsa-miR-335-3p, hsa-miR-342-3p, hsa-miR-644b-3p, hsa-miR-491-3p, hsa-miR-4732-3p were downregulated in patients where RS was involved as compared to AC. The expression of hsa-miR-141-3p was upregulated in patients where RS region was involved as compared to AC. Analysis of the registered UC patient's database from the hospital revealed that the site of CRC was predominantly the rectosigmoid region of the colon in most of the cases. This is the first study to show the differential expression of miRNA involving different sites of colon in UC patients. Taking our data and previous reports into consideration, we propose that differential miRNA expression during UC perhaps contribute in the development of UC associated CRC at the rectosigmoid area.

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Evaluation of gastroprotective effects of aqueous stem bark extract of *Ziziphus jujuba* L., against HCl/ethanol-induced gastric mucosal injury in rats

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Introduction: *Ziziphus jujuba* stem bark is used in Iranian traditional medicine as a treatment of many diseases specially, gastrointestinal disease and wound healing. Based on traditional books, the present investigation evaluated the gastro protective effects of standardized aqueous extracts of *Z. jujuba* stem bark against acidified ethanol-induced gastric ulcers as well as anti-helicobacter pylori activity of the plant extract.

Materials & Methods: Five groups of rats were orally pre-treated with normal saline (0.9%) as ulcer group, 150 mg/kg of ranitidine as positive group, 100 mg, 200 mg and 400 mg of standardized extract solution as the experimental groups, respectively. Two hours later, acidified ethanol solution was given orally in order to induction of gastric ulcer. Antibacterial against clinical strains of *H. pylori* evaluated through disc diffusion method.

Results: Ulcer group exhibited significantly severe mucosal injury as compared with ranitidine or extract which shows significant protection towards gastric mucosal injury the plant promotes ulcer protection as it shows significant reduction of ulcer area, and histology showed marked reduction of edema in mucosal and submucosal layer compared with ulcer group. *Z. jujuba* stem bark extract had no effects against on *H. pylori*.

Conclusion: The present study indicates that *Z. jujuba* stem bark extract have potential antiulcer activity which might be due to its anti-secretory activity and increased resistance to necrotizing agents, providing a direct, protective effect on the gastric mucosa. Our study showed that anti- *H. pylori* activity is not among gastroprotective mechanism of *Z. jujuba*. Further pre-clinical and clinical investigation for evaluating natural active agents and efficacy of this plant is recommended.

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October 24-25, 2016 Valencia, Spain

Endometriotic cyst mimicking a retroperitoneal tumor – A rare scenario

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Ectopic endometrial tissues are rarely observed on the serosal surfaces of bowel and laparotomy incisions, in the lungs, bones and in the urinary tract. A few case reports of endometriosis in the retroperitoneal location has been reported in the English literature. Endometriotic cyst in a retroperitoneal location mimicking a retroperitoneal tumor through the mesentery of sigmoid colon is an extremely rare presentation. A 45 year old woman presented with pain abdomen of 3 months duration. CT abdomen & pelvis revealed a retroperitoneal mass adjacent to left psoas and left ureter. On laparotomy, a cystic mass was found in the retroperitoneum over the left common iliac vessels. The mass was excised in to preserving the left ureter, left iliac vessels and sigmoid colon. The final histopathology revealed an endometriotic cyst. Recto-sigmoid junction is the most common site of extra-genital endometriosis, with less frequent sites being the rectovaginal septum, small intestine, cecum and appendix. Retroperitoneal presentation of endometriotic cyst is a rare presentation and only few cases have been reported. Retroperitoneal endometriotic cyst may mimic a retroperitoneal tumor in view of the location. Retroperitoneal endometriotic cyst in the sigmoid mesentery is an extremely rare presentation. Whenever a CT guided biopsy was not diagnostic in a retroperitoneal lesion, complete excision is the treatment of choice to arrive at a final diagnosis.

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Assessment of the therapeutic effect of allopurinol on patients with non-alcoholic fatty liver disease associated with hyperuricemia by cytokeratin 18

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Background: Non-alcoholic fatty liver disease (NAFLD) is the most common cause of chronic liver injury. Elevated uric acid (UA) is an important factor in the development of NAFLD. Both combined result in apoptosis which is an important mechanism in pathogenesis of NAFLD, where it leads to activation of caspase family of intracellular proteases which then cleave different intracellular proteins including cytokeratin 18 (CK18) which can be used as a key marker in NAFLD.

Objective: The objective of this study is to evaluate the effect of treating hyperuricemia by allopurinol on NAFLD patients by blood markers as CK18, liver enzymes (GOT, GPT), cholesterol (Chol) and triglyceride (TG).

Methods: In this study, 31 hyperuricemic patients with NAFLD diagnosed by ultrasound were enrolled in the study and divided into two groups; Group A (14 patients): Placebo group who received starch based tablets for 3 months and Group B (17 patients): Treatment group who received allopurinol (300 mg) for 3 months. UA, CK 18, GPT, GOT, Chol and TG were measured before and after treatment.

Results: The study showed a significant decline in CK18 levels after treatment ($P=0.006$), improvement in GPT and GOT levels after treatment ($P<0.001$ and $P=0.013$, respectively), also there was an improvement in Chol and TG levels after treatment ($P=0.01$ and 0.038 , respectively).

Conclusion: Allopurinol may play a role in improvement of patients with NAFLD associated with hyperuricemia and CK18 may be used as a good marker in assessing patients' improvement.

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October 24-25, 2016 Valencia, Spain

Laparoscopic uncut Roux-en-Y anastomosis in the distant gastrectomy for gastric cancer: A report of 92 patients

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Objective: The aim of this study was to investigate the safety and feasibility of laparoscopic uncut Roux-en-Y anastomosis in the distant gastrectomy for gastric cancer.

Methods: The clinical data of 92 patients performed laparoscopic uncut Roux-en-Y anastomosis in the Department of Gastric Surgery, the First Affiliated Hospital of Nanjing Medical University from June 2014 to June 2016 were analyzed retrospectively.

Results: The operations were performed successfully for all patients. The mean operation duration, anastomosis time, blood loss and the number of lymph nodes dissection during the surgery were (178.67 ± 29.12) min, (30.84 ± 7.41) min, (48.78 ± 35.64) ml and 34.43 ± 9.84 respectively. The time spent before gastrointestinal motility, liquid-diet intake, out-of-bed ambulation and the average hospitalization days after operation were (76.40 ± 21.47) hours, (5.30 ± 1.25) days, (48.14 ± 20.25) hours and (9.19 ± 3.09) days respectively. Postoperatively, 6 patients experienced complications, including gastrointestinal bleeding (2 patients), duodenal stump fistula (1 patient), Chylorrhea (1 patient), Roux-Y stasis syndrome after gastrectomy (2 patients), all of the complications were cured conservatively. None of the other complications occurred, such as anastomotic fistula, anastomotic stenosis, infection of incision, etc.

Conclusion: The laparoscopic uncut Roux-en-Y anastomosis is safe and feasible in the distant gastrectomy with D2 dissection for gastric cancer, with advantages of less trauma, faster recovery and so on.

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Standardization of an isolation protocol of group A rotaviruses among neonatal diarrheic calves, Morocco

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Group A rotaviruses (RVA) are the main cause of neonatal calve diarrhea (NCD) in Morocco. Until now, no reports are available regarding isolation and cultivation of RVA in clinical samples from Moroccan domestic animals or children with acute gastroenteritis (AGE) and burden due to this infection in animals remain unknown. Hence, this study aims to isolate RVA strains from NCD clinical samples in order to support RVA disease control in Morocco. This isolation process constitutes a first step toward vaccine development. Thirteen fecal samples were obtained from calves with a single episode of neonate calf diarrhea at three different dairies and two samples were collected from field during a severe NCD outbreak. Diagnosis of RVA infection was based on fecal immune-chromatographic rapid test and further evaluated for their hemagglutination (HA) activity. RVA isolation was carried out on MA104 cells after inoculates were treated with different concentrations of trypsin TPCK. All RVA isolates were confirmed by LSI VetMAX™ Triplex Ruminant Rotavirus and Coronavirus Real-Time PCR kit. RVA isolation was achieved for nine clinical samples following one or two passages (60%) and was properly depended on HA activity and trypsin treatment of inoculates. The first sign of CPE detected consisted of increased cell granularity, obscure cell boundaries, cell rounding, and eventual degeneration and detachment of cells. These results constitute a crucial and a necessary step allowing preventive and veterinary medicine to support RVA disease controls in the country.

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October 24-25, 2016 Valencia, Spain

Adiponectin, Leptin, IGF1 and TNF α serum biomarkers for non-invasive diagnosis of colorectal adenoma

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Background and Aim: The potential role of Adiponectin, Leptin, IGF1 and TNF α as biomarkers in colorectal adenoma is not clear. Therefore, we aimed to investigate the blood serum levels of these biomarkers in colorectal adenoma.

Method: The case-control study consisted of serum from 180 African American patients with colon adenoma (cases) and 198 healthy individuals (controls) at Howard University Hospital. We used ELISA for Adiponectin, Leptin, IGF1 and TNF α detection and quantification. Statistical analysis was performed by t-test and multivariate logistic regression.

Results: The respective differences in median Leptin, Adiponectin, IGF1 and TNF α levels between control and case groups (13.9 vs. 16.4), (11.3 vs. 46.0), (4.5 vs. 12.9) and (71.4 vs. 130.8) were statistically significant ($p < 0.05$). In a multivariate model, the odds ratio (ORs) for Adiponectin, TNF α and IGF1 were 2.0 (95% CI=1.6–2.5; $P < 0.001$), 1.5 (95% CI=1.5– 2.0; $P = 0.004$) and 1.6 (95% CI=1.3–2.0; $P < 0.001$), respectively. There was a positive correlation between serum Adiponectin and IGF1 concentrations with age ($r = 0.17$, $P < 0.001$ and $r = 0.13$, $P = 0.009$), TNF α , IGF1 and Leptin concentration with Body Mass Index (BMI) ($r = 0.44$, $P < 0.001$; $r = 0.11$, $P = 0.03$ and $r = 0.48$, $P < 0.001$), respectively. Also, there was a negative correlation between Adiponectin and Leptin concentration with BMI ($r = -0.40$, $P < 0.001$ and), respectively.

Conclusion: These data support the hypothesis that Adiponectin, IGF1 and TNF α high level are increasing the risk of colon adenoma and can be applied for colorectal adenomas risk assessment.

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Evaluation of the impact of pre and post-transplant metabolic derangements on the neurological complications following liver transplantation

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Neurologic complications after liver transplantation are a major source of morbidity and mortality and proper prediction for those at risk may help in improving the outcome. The results of our study showed that severity of end stage liver failure prior to transplantation might be the most common risk factor for the development of post-transplant neurological complications and careful evaluation of other risk factors may be required for those patients in order to decrease the incidence of complications. Still the use of tacrolimus is associated with risk of neurological complications and reduction or discontinuation of tacrolimus lead to improvement of neurological complications. According to our study, electrolytes and metabolic derangements are not risk factors for development of neurological complications. Although, the risk of neurological complications in our series is high but there was no impact on the survival.

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9TH EURO GLOBAL GASTROENTEROLOGY CONFERENCE

October 24-25, 2016 Valencia, Spain

Calretinin Expression in Hirsch sprung Disease – A Potential Marker of Ganglion Cells

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Statement of problem: Hirschsprung disease (HSCR) or congenital intestinal aganglionosis is a birth defect characterized by complete absence of neuronal ganglion cells from a portion of the intestinal tract, mostly in a segment of rectum and variable length of contiguous proximal, causing functional obstruction and colonic dilation proximal to affected segment. (Amiel and Lyonnet, 2001) Routine diagnostic modalities like Haematoxylin & Eosin (H&E) and Acetylcholine Esterase (AChE) staining as well as radiology-based clinical techniques have been conventionally used for identification of aganglionosis and presence of hypertrophic nerve trunks in the affected segment as primary indicators of HSCR. (Kacar et al., 2012) However, these conventional methods have their inherent deficiencies as H&E requires multiple trans-mural biopsies and the interpretation of ganglion cells is often very difficult. (Tabbers et al., 2014) Similarly, AChE requires fresh frozen section for which the chances of technical error are very high and this facility is not commonly available in Pakistan. The number of misdiagnosed results with potential overtreatment stands in need for reliable staining to prevent harm from unnecessary surgery and mortality. Recently, Immunohistochemical markers are being increasingly used and evaluated in Pathology laboratories. No immunohistochemical marker, either alone or in combination, has emerged from those researches that are as promising as Calretinin. Hence, this study was designed with an aim to observe the immunohistochemical expression of Calretinin as a marker for aganglionosis and to detect ganglion cells in the affected areas for better and more accurate diagnosis of the disease.

Methodology: This study was conducted at University of Health Sciences Lahore, Pakistan from February to September, 2016. Colonic Biopsy Specimens from 73 patients collected mostly from Mayo Hospital, Lahore with established histopathologic diagnosis of HSCR were considered for the study. Age range was 0.1-120months. There were 48(65.8%) cases who were ≤ 12 months old, 20(27.4%) were 12.1-60 months old and 5(6.8%) of the cases were 60.1-120 month old. The mean age of patients was 12.52 ± 9.21 months. There were 52(71.23%) male and 21(28.77%) female patients. The male to female ratio in this study was 2.48:1. According to sign and symptoms and clinical examination, 69(94.5%) cases had mostly long standing constipation, 47(64.4%) cases had fever, 68(93.2%) cases had vomiting, 31(42.5%) cases had failure to thrive, 20(27.4%) cases had Enterocolitis and 63(86.3%) of the patients had palpable abdominal masses. Methodology involved staining of fresh sections with H&E procedure for provisional histological diagnosis. The biopsies were then processed for immunohistochemical staining with Calretinin and were observed for presence of ganglion cells.

Findings: All the ganglion cells took brownish-black stain and were easily identified, which were not being identified on H&E. Ganglion cells were present and absent in 42(57.53%) and 31(42.47%) respectively. The study revealed that the Calretinin immunohistochemistry was very sensitive and specific for detecting ganglion cells.

Conclusion and significance: It was concluded that Calretinin provides a very reliable and cost effective adjunctive test to be routinely used with H&E in the evaluation of Rectal Section Biopsies (RSBs) for HSCR. The use of Calretinin may help the Pathologists in making accurate and reliable diagnosis for HSCR and consequently eliminating the need for repeated biopsies and unnecessary surgeries.

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