**THE GIST OF IT: KIT AND PDGFRα MUTATION TESTING FOR GIST PATIENTS**

**Babb C, Schnugh D, Willem P**

Gastro-intestinal stromal tumour (GIST) is the most common mesenchymal tumour of the gastro-intestinal tract. Since the introduction of tyrosine kinase inhibitors (TKIs), such as Gleevec®, the treatment of these patients has improved dramatically. Heterogenic mutations in the KIT and PDGFRα genes are central to the pathogenesis of GIST. The presence of these mutations is the rationale for TKI therapy. Previous studies in other regions of the world have shown that the commonest mutation occurs in KIT exon 11 and varies from substitutions to deletions to insertions. Most of these mutations indicate that the patient will respond well to Gleevec® therapy. Another common mutation, represented by a duplication in KIT exon 9, is an indicator that the patient requires a double dose of Gleevec® to get a similar response to, if not the same as, patients who have a KIT exon 11 mutation. The test has been established at the Somatic Cell Genetics Unit, Department of Haematology and Molecular Medicine, National Health Laboratory Service, providing this key service to treating physicians in South Africa.

DNA was extracted from paraffin-embedded resected tumour specimens, and gene-specific exons were amplified by the polymerase chain reaction (PCR). Mutational screening of exons in the KIT and PDGFRα genes was done by direct sequencing of the PCR products. As there are a number of exons (21 in total) to be screened, a priority list, based on previously reported frequency of exon mutations, was determined to shorten the turnaround time.

A total of 17 GIST tumour biopsies from South African patients have been tested. They include a sample from a juvenile boy and a patient suffering from neurofibromatosis 1 (NF1). There were 8 females and 9 males, and the median age (excluding the 14-year-old) was 58 years. The most common site of disease was the stomach. Mutations were mainly detected in KIT exon 11, with 7 deletions, 1 deletion-insertion and 4 substitutions, most frequently affecting codons 557 - 560. The remaining mutation detected was a deletion in PDGFRα exon 18. Four patients had no detectable mutations in the exons screened and were considered to have wild-type disease. These included the juvenile and the NF1 patient, which is in keeping with what is generally observed in these GIST patients. One unknown and 4 known silent polymorphisms were observed within the exons sequenced. This was not surprising, as black African populations are known to have more polymorphisms.

The mutational screening of KIT and PDGFRα genes informs treatment decisions for GIST patients. With this test now available in South Africa, the management of patients with this rare disease can improve significantly. The trend of mutations observed in this preliminary study in Africa predicts that patients should respond well to Gleevec® therapy. This study establishes baseline data on the molecular profile of GIST in a South African population.

**THE EFFICACY OF PROFOUNDED ACID INHIBITION WITH ESOMEPRAZOLE 40 MG BD TO REVERSE C-MYB mRNA OVER-EXPRESSION IN PATIENTS WITH BARRETT’S OESOPHAGUS**

**Marais M, Kidd M, Abbas Z, Parker I M, Kotze M J, Van Rensburg C J**

**Background:** The role of c-myc mRNA expression in Barrett’s oesophagus has been elucidated and demonstrates a progressive and significant increase in histopathologically worse tissue type. Currently life-long proton pump inhibition is recommended, but data to support the effectiveness of this practice are lacking and mostly indirect.

**Aim:** To study the efficacy of 3 months’ profound acid inhibition (esomeprazole 40 mg bd) in reversing c-myc mRNA over-expression in patients with Barrett’s oesophagus.

**Subjects and methods:** Seventeen patients (12 males, 5 females, mean age 63 years, BMI 27.7) with histologically confirmed Barrett’s oesophagus were treated with esomeprazole 40 mg bd for 12 weeks. Oesophageal biopsies were obtained pre-treatment from both the Barrett’s epithelium and the adjacent normal squamous mucosa and repeated after 3 months’ treatment. C-myc mRNA expression was determined by RT-PCR. Statistical analysis was performed using one-way analysis of variance, the chi-square, Kruskal-Wallis and Mann-Whitney tests and the nominal p-value.

**Results:** Pre-treatment there was a statistically significant difference in c-myc mRNA expression between the Barrett’s and the normal squamous epithelium (p=0.01). There was a statistically significant decrease in c-myc mRNA expression after 3 months’ treatment in the Barrett’s epithelium (p=0.02), but this was not observed in the normal squamous epithelium.

**Conclusion:** The c-myc mRNA expression significantly decreased after 3 months’ treatment with esomeprazole 40 mg bd. This change was not observed in the normal squamous epithelium.

**STUDY OF OESOPHAGEAL STRICTION DILATATION AT NELSON MANDELA ACADEMIC HOSPITAL**

**Bhattarai P R**

**Background:** Oesophageal strictures are common in the Transkei region, which is known for its high incidence of oesophageal carcinoma. The majority of strictures are caused by malignant disease, with more than a third of patients who are scoped requiring palliative dilatation. Patients with oesophageal strictures
present in a poor general condition, and perforation of the oesophagus in such cases makes the prognosis even worse.

**Aim:** To review all cases of oesophageal dilatation and attempt to correlate oesophageal perforation with different procedures and patient disease factors.

**Methods:** All patients with oesophageal strictures who underwent dilatation in the Department of Surgery from November 2008 to April 2010 were included in this study. Data were recorded at the time of the procedure and patients were followed up in the ward until discharge or death. Patients were dilated either using a balloon dilator through a flexible scope or with Savary Gillard dilators through a rigid oesophagoscopy.

**Results:** A total of 242 procedures were done in 218 patients over the study period (126 males and 116 females, age range 22 - 103 years, mean age 62.6 years, 24 procedures for benign and 218 for malignant strictures; 59 patients underwent Savory Gillard dilation through a rigid oesophagoscopy and 183 dilations were done with a balloon dilator through a flexible scope). A total of 5 perforations occurred, 1 for 24 benign oesophageal strictures and 4 for 218 malignant oesophageal strictures.

**Conclusions:** Oesophageal dilatation is a safe procedure with good palliation in a resource-limited area.

**Category:** Liver

**HEPATIC TB-ASSOCIATED IRIS COMPARED WITH ANTIRETROVIRAL-NAÏVE HIV POSITIVE PATIENTS WITH HEPATIC TB**

**Sonderup M, Hairwoodzi H, Spearman W, Wainwright H**

**Introduction:** The immune reconstitution inflammatory syndrome (IRIS) is an important early complication of antiretroviral therapy (ART) in resource-limited settings, particularly in patients with TB. IRIS is a consequence of the rapid restoration of pathogen-specific immune responses to opportunistic infections causing deterioration in treated infection or a new presentation of subclinical infection. Few data exist regarding the clinical and pathological features of patients with hepatic manifestations of TB IRIS and how this compares with ART-naive HIV/AIDS patients with liver TB, or on what features suggest IRIS as the reason for the liver disease.

**Methods:** Patients who had undergone liver biopsy and fulfilled consensus definitions for TB IRIS were retrospectively selected. A control group of ART-naive patients with liver TB were selected. All biopsies were performed using a standard needle biopsy set. Clinical data were obtained from patient records and liver biopsies were assessed blindly.

**Results:** 22 patients in the TB IRIS and 11 in the TB liver group were evaluated (mean age 31.8±4.9 and 36.2±13.3 years, p=0.2). The pre-ART median CD4 count was 34 cells/µl (8 - 175) in the TB IRIS group and 61 (17 - 118) in the ART-naive TB liver group (p=0.08). In the TB IRIS group the median change in CD4 count from the lowest pre-ART nadir was 115 (36 - 344), while the median duration of ART was 30 (14 - 71) days before presentation. In the TB IRIS group all presented with hepatomegaly. The median ALT, AST and ALP values were not significantly different between the two groups, but GGT was higher in the TB IRIS (1 004, range 190 - 2 161) than in the TB liver group (313, range 167 - 1 483) (p<0.007). Histological examination revealed significantly more granulomas per liver core in the TB IRIS group than in the TB liver group (26 (4 - 111) v. 7 (3 - 25), p=0.006). Associated with the granulomas, eosinophils were observed more frequently in the TB IRIS group than in the TB liver group (86% v. 27%, respectively).

**Conclusion:** Hepatic TB IRIS occurs early in the course of ART. Features suggesting IRIS include hepatomegaly, rapid CD4 increase and a significantly elevated GGT. Histologically suggestive features include the presence of numerous granulomas with an eosinophilic inflammatory component.

**AZATHIOPRINE- OR 6-MERCAPTOPURINE-ASSOCIATED HEPATOTOXICITY DIMINISHES UPON ADMINISTRATION OF 6-THIOGUANINE IN IBD PATIENTS**

**Van Asseldonk D, Mulder C J, Van Bodegraven A A**

**Aim:** A skewed metabolism with subsequently high levels of 6-methylmercaptopurine nucleotides (6-MMP) upon administration of azathioprine or 6-mercaptopurine has previously been related to hepatotoxicity. We hypothesised that 6-thioguanine (6-TG) therapy, which is not accompanied by the formation of these 6-MMP, could ameliorate or avoid hepatotoxicity.

**Materials and methods:** From a cohort of IBD patients which has been treated with 6-TG, patients who previously failed AZA or 6-MP as a result of a skewed metabolism were selected. Laboratory test- and therapy-specific data were collected at baseline and during follow-up.

**Results:** Eleven patients (3 males) with a mean age of 50.2 (SD 12.6) years were included in the analysis. Five had Crohn’s disease and 6 had ulcerative colitis. Just before initiation of 6-TG the median 6-MMP/6-TGN ratio was 48 (19 - 124). Median 6-TG dosage was 21 mg (range 10 - 24) daily and the median time to follow-up was 2.5 months (1.4 - 18.2). At follow-up 2 out of 11 had liver test abnormalities compared with 8 out of 11 at baseline (p=0.014). Mean ALAT and ASAT concentrations decreased from 34 to 22 U/l (p=0.038) and 75 to 27 U/l (p=0.014), respectively. The median 6-TGN concentration was 300 pmol/8x108 RBC (170 - 830) at baseline, whereas at follow-up it was 1 070 (390 - 2 100) (p=0.001). Both at baseline and during follow-up all but one of the patients were in clinical remission.

**Conclusion:** Hepatotoxicity associated with skewed thiopurine metabolism is reduced in IBD patients given 6-TG. This may be because 6-TG administration does not cause MMP formation.

**BACTERIAL TRANSLOCATION, THE CAUSE OF ACTIVATED INTESTINAL MACROPHAGES IN DECOMPENSATED LIVER DISEASE**


**Background:** Bacterial infections are a well-described complication in chronic liver disease (CLD). In fact the decomposition of liver functions can occur as a result of bacterial products and DNA. However, the exact mechanism of bacterial translocation (BT) is unknown.
Aim: To study the role of epithelial barrier and innate immune response in BT associated with CLD.

Materials and methods: Decompensated CLD (N=38) patients and controls (N=9) were included. Plasma LPS levels were determined. At endoscopy duodenal biopsies were obtained for histology, electron microscopy, macropathie and RNA isolation. Flow cytometry on isolated macrophages as well as qRT-PCR on total RNA were performed.

Results: Plasma LPS levels were elevated in decompensated CLD. EM showed intact epithelial barriers and tight junctions in both CLD patients and controls. FACS showed that isolated intestinal macrophages in CLD were activated (CD14+, Trem+, CD80+, CD66+). 11 genes including IL-8, NOSII, CXCL1, CXCL6, CCL13 as well as TLR1 and TLR6 were found to be up-regulated in CLD.

Discussion: BT leads to decompensation of liver function in CLD. The importance of BT is reflected in elevated plasma levels of LPS in CLD. Isolated intestinal macrophages in CLD but not in controls were activated (CD14+), confirming recruitment of circulatory monocytes. The upregulation of IL-8 and other chemokines is likely to result from the interaction of bacterial products with TLR 1 and 6 on epithelial cells. Furthermore, NOSII was upregulated and has been shown to disrupt epithelial barrier function, which may directly impact on BT. This study showed that activated intestinal macrophages may play a key role in BT in CLD.

LIVER HISTOLOGY OF IBD PATIENTS WHO ARE TREATED WITH 6-THIOGUANINE DUE TO FAILURE OF CONVENTIONAL THIOPURINES REVEALS VERY FEW CASES OF NODULAR REGENERATIVE HYPERPLASIA


Aim: The aim of this study was to assess short-term hepatotoxicity of 6-TG therapy in a large population of IBD patients previously failing conventional thiopurines.

Materials and methods: A cross-sectional multi-centre cohort study was performed including IBD patients treated with 6-TG for at least 6 months and who underwent a liver biopsy for safety assessment. The liver specimens were fixed with H&E, trichrome and reticuline and were scored by experienced liver pathologists.

Results: Liver biopsy specimens were obtained from 99 patients with a mean age of 43.8 years (SD 12.0). Thirty-six patients were male. All but 2 patients were pretreated with azathioprine and/or 6-mercaptopurine. Mean 6-TG dose was 0.28 mg/kg (SD 0.07) and median 6-TG treatment duration, from initiation up to the first liver biopsy, 25 months (range 6 - 65). Liver histology revealed no abnormalities in 51 specimens (51.5%), mild steatosis in 14 (14.1%), mild fibrosis in 3 (3.0%), severe steatosis in 2 (2.0%), steatohepatitis in 2 (2.0%), sinus dilatation in 8 (8.1%), cholangitis/PSC in 4 (4.0%), a specific regeneration in 11 (11.1%), and nodular regenerative hyperplasia (NRH) in 4 (4.0%).

Conclusion: NRH (4%) is an uncommon finding in IBD patients who had been failing conventional thiopurine therapy and were subsequently treated with 6-TG. This is in contrast to some previous studies (up to 62%), but corresponds with the prevalence of NRH in thiopurine-naive IBD patients (6%).

RISK FACTORS FOR EARLY REBLEEDING AND DEATH IN ALCOHOLIC CIRRHOTIC PATIENTS WITH ACUTE VARICEAL HAEMORRHAGE TREATED WITH EMERGENCY ENDOSCOPIC INJECTION SCLEROTHERAPY


Background: Bleeding from oesophageal varices is a leading cause of death in alcoholic cirrhosis. Recurrent bleeding and subsequent progressive liver failure result in significant morbidity and mortality.

Aims: Identification of risk factors for early rebleeding and death at 6 weeks after endoscopic injection sclerotherapy.

Methods: A retrospective evaluation was performed on a prospectively collected database of 310 consecutive alcoholic cirrhotic patients with AVH treated at a single centre to identify risk factors related to rebleeding and death within 6 weeks of initial treatment.

Results: 310 alcoholic cirrhotic patients with AVH underwent 786 endoscopic varical injection treatments (342 emergency, 444 elective) during 919 endoscopy sessions in the 6 weeks after their first variceal bleed. Sclerotherapy controlled initial AVH in 204 patients (98%). 75 (24.2%) patients rebled. Of 15 variables studied, bilirubin levels >51 mmol/l and >6 units of blood transfused during initial hospital admission were predictors of variceal rebleeding. Mortality increased exponentially as the Child-Pugh score increased. Encephalopathy, ascites, bilirubin levels >51 mmol/l, INR >2.3, albumin ≤2.5 mg/dl and the need for balloon tube tamponade were predictors of death within the first 6 weeks.

Conclusion: Endoscopic sclerotherapy controls acute oesophageal variceal bleeding in most alcoholic cirrhotic patients, with a rebleeding rate of 24.2%. At 6 weeks overall survival was 75.2%. Most deaths occur in Child-Pugh grade C patients. Patients with AVH and encephalopathy, ascites, bilirubin levels >51 mmol/l, INR >2.3, albumin ≤2.5 mg/dl and who require balloon tube tamponade are at increased risk of dying within the first 6 weeks.

Category: Hepato-biliary

MALIGNANT BILIARY OBSTRUCTION: A PROSPECTIVE RANDOMISED TRIAL COMPARING PLASTIC AND METAL STENTS FOR PALLIATION OF SYMPTOMATIC JAUNDICE

Bernon M, Bornman P C, Burmeister S, Krige J E J, Shaw J M

Background: Both plastic and self-expanding metal stents (SEMS) have been used to relieve jaundice in patients with advanced malignant biliary obstruction. This study compared the clinical efficacy of plastic versus metal biliary stents.

Materials and methods: In a prospective randomised controlled trial 22 patients with malignant common bile duct obstruction not amenable to curative resection were offered palliative stenting from November 2008 to March 2010 and were followed up until death. Data were collected prospectively. We compared patient survival and stent patency rates.

Results: 12 patients received 10 Fr plastic stents and 10 patients received expandable metal stents. Mean duration of hospital stay after stenting for both groups was 2 days (range 1 - 2 days). Jaundice was relieved in all patients. Two patients with metal
stents required subsequent intervention at 8 and 21 days: one stent blocked due to a bile duct stone, and another migrated proximally and was replaced. Plastic stents in 6 patients blocked at a mean of 7 months (range 3 - 18 months) in the metal stent group 2 patients required re-admission twice to hospital (total 32 days) compared with the plastic group in which 5 patients required a total of 36 days in hospital. Mean survival was 173 days compared with 192 days.

Conclusion: Compared with SEMS, plastic 10 Fr biliary stents blocked more frequently, were replaced more often and required more hospital admissions but necessitated a similar total number of days in hospital after placement. These preliminary data suggest only a marginal advantage for palliative metal stenting.

**COMBINED PALLIATIVE STENTING FOR MALIGNANT BILIARY AND DUODENAL OBSTRUCTION**


**Background:** Biliary and duodenal stenting provides effective palliation for patients who have malignant biliary or duodenal obstruction. This study evaluated the clinical efficacy of combined palliative stenting in patients with advanced biliary and duodenal malignant obstruction.

**Patients and methods:** Consecutive patients with advanced biliary and duodenal malignant obstruction not suitable for surgical bypass referred for palliative duodenal stenting using self-expanding metal stents (SEMS) and biliary stenting using either SEMS or 10 or 12 Fr plastic stents were followed prospectively from January 2009 to March 2010. Stenting was performed under fluoroscopic guidance and conscious sedation. Percutaneous transhepatic stenting was used when initial endoscopic biliary access was not technically possible. Data were collected prospectively. Demographic data, nature of the malignant stricture, stent deployment success rates, stent patency, procedural complications and survival time were recorded.

**Results:** Forty-two patients (pancreatic carcinoma N=31; cholangiocarcinoma N=4; gallbladder carcinoma N=3; antral gastric carcinoma N=4) underwent double stenting. In 40 patients the biliary obstruction occurred before the onset of duodenal obstruction, and in 2 patients the duodenal obstruction preceded biliary obstruction. The mean pre-stenting bilirubin level was 297 µmol/l and the gastric outlet obstruction severity score (GOOSS) 0. Duodenal stenting was successful in all 42 patients; in 3, oral intake after stenting was inadequate. Endoscopic biliary stents were placed in 33 patients (SEMS N=29, plastic N=4) and 9 biliary stents were inserted using radiological percutaneous transhepatic biliary access (SEMS N=7, plastic N=2). Mean hospital stay for each procedure after stenting was 3.8 days. The functional success rate with relief of jaundice was 95% (40/42) and 93% of patients (39/42) had improved GOOSS scores. Complications occurred in 3 patients with duodenal stents (GI bleeding in 2, stent migration in 1). During follow-up, 5 duodenal stents and 5 biliary stents blocked. The median survival after combined stenting was 85.2 days (range 4 - 320 days).

**Conclusion:** Biliary and duodenal stenting is safe and effective in malignant biliary and duodenal obstruction and provides effective palliation in patients with advanced malignancy who are unsuitable for bypass surgery and have limited life expectancy.

**Category:** Small bowel/inflammatory bowel

**AUTOLOGOUS STEM CELL TRANSPLANTATION IN REFRACTORY COELIAC DISEASE TYPE II PATIENTS UNRESPONSIVE TO CLADRIBINE THERAPY**


**Background:** Autologous haematopoietic stem cell transplantation (auSCT) is used for T-cell eradication in both malignant and immunological diseases. It seems feasible and safe for refractory coeliac disease (RCD) type II on the basis of short-term follow-up, although long-term results have not been evaluated yet. Transition into enteropathy-associated T-cell lymphoma (EATL) occurs in 60 - 80% of cases, with a high mortality rate. It is therefore important to evaluate new treatment strategies.

**Methods:** Between March 2004 and February 2010, we intended to treat 18 RCD II patients with auSCT preceded by conditioning with fludarabine and melphalan, as a consequence of unresponsiveness to cladribine therapy. Adverse events, survival rate, EATL development, and change in clinical, histological and immunological course were monitored.

**Results:** Thirteen patients were transplanted successfully and followed for >2 years. Three of them died. The 4-year survival rate was 66%. The majority showed an impressive clinical improvement and 5 complete histological remission. In 6 patients auSCT could not be performed; they all died with a median survival of 5.5 months. EATL was observed in 1 transplanted patient, only after 4 years of follow-up.

**Conclusion:** AuSCT after conditioning with high-dose chemotherapy in RCD II patients unresponsive to cladribine therapy is feasible, and seems promising.

**MORTALITY IN AN IBD COHORT FROM CAPE TOWN**

**Epstein D, Levin D, Watson I K, Watermeyer G**

No mortality data on inflammatory bowel disease (IBD) patients from South Africa have been published. Controlled population-based studies from the developed world have not consistently shown that IBD causes premature death.

A retrospective analysis of all IBD patients on the Groote Schuur Hospital (GSH) IBD database was conducted. Patient deaths were identified on the GSH Clinicom System and IBD patient death notifications were also checked on Ancestry24.

Clinical record review was performed and cause of death categorised as:
1. IBD related
2. Non-IBD cancer
3. Other cause of death
4. Unknown.

**Results:** 1 464 patients with IBD were reviewed, consisting of 690 patients with Crohn’s disease (47%) and 774 with ulcerative colitis.
and indeterminate colitis (53%). 84 (5.7%) deaths were recorded. In the ulcerative colitis group, 13 deaths were IBD related, 5 due to non-IBD cancer, 4 due to other causes and 19 due to unknown causes. In the Crohn’s disease group the respective figures were 12, 1, 4 and 25. The IBD-related deaths were due to IBD cancer (6), peri-operative (15), FSC related (3) and due to long-term TPN (1).

Conclusion: This is the first retrospective analysis of IBD-related mortality from southern Africa.

PREGNANCY WEIGHT GAIN AND BIRTH OUTCOME BY NUTRITION EDUCATION

Jahan K

Rationale and objectives: About 35% of babies born in Bangladesh are of low birth weight (LBW). The objective was to assess the effect of nutrition counselling on reduction in LBW and increase in weight gain during pregnancy.

Materials and methods: 300 pregnant women in the 3rd trimester were randomly allocated to a control group or an intervention group that received education on food security, disease control and care, and appropriate breastfeeding of the newborn.

Results and findings: The mean weight gain of pregnant women was higher in intervention group compared with controls (8.58 kg v. 6.08 kg; p=0.001). The prevalence of LBW was significantly lower in the intervention group compared with the control group (9 v. 5.3%). Early initiation of breastfeeding was also higher in the intervention group (71% v. 7.3%; p=0.001).

Conclusion: This study demonstrated that nutrition education can effectively reduce low birth weight.

Category: Colorectal

DOUBLE VERSUS SINGLE SAMPLING OF FECAL IMMUNOCHIMICAL TESTS FOR COLORECTAL CANCER SCREENING: ADDED VALUE OR ADDED COSTS?


Background: Faecal immunochemical tests (FITs) are widely used in colorectal cancer (CRC) screening and have relatively good performance. Yet, as sensitivity is well below 100%, there is room for improvement. The aim of the present study was to investigate whether FIT sampling from bowel movements on 2 consecutive days can improve sensitivity without substantially affecting specificity.

Methods: In subjects scheduled for colonoscopy, test performance of single FIT sampling was compared with 2-day FIT sampling. Double FIT sampling was considered positive if one or both FITs was higher than the cut-off value. Test performances were evaluated at cut-off values ranging from 50 to 150 ng/ml (incremental steps of 25 ng/ml).

Results: Of 1,096 subjects who performed two FITs and underwent total colonoscopy, 124 (11.3%) had screening relevant neoplasia, of which 20 were CRC stage I or II and 104 were advanced adenomas. Positivity rates for single FIT ranged from 10% to 16%, and for double FIT from 12% to 21%. At the same cut-off value for positivity, sensitivity of double FIT sampling was higher than sensitivity of single FIT sampling. For any particular specificity (e.g. 90%), the sensitivity of double FIT was slightly higher (52%, cut-off 100 ng/ml) than that of single FIT (46%, cut-off 75 ng/ml) at a lower cut-off value, but these differences were not statistically significant.

Conclusions: Two-fold sampling of FIT increases sensitivity for advanced neoplasia. However, at a given specificity, sensitivity of double sampling is comparable to single sampling at a lower cut-off value.

A PROSPECTIVE STUDY OF CLOSTRIDIUM DIFFICILE-ASSOCIATED DIARRHOEA AT A TERTIARY REFERRAL HOSPITAL IN SOUTH AFRICA

Rajabally N, Mendelson M, Oliver S, Pentecost M, Pretorius G, Watermeyer G, Whitelaw A

Objective: To report the incidence of CDAD at GSH, identify risk factors, assess patient outcomes and determine the presence of NAPI.

Methods: Adult patients with diarrhoea seen over 15 months were included prospectively. Stools were tested for C. difficile toxin A using standard EIA. Positive specimens were evaluated for NAPI by real-time PCR.

Results: 653 stools were analysed; complete data were available for 645. CDAD was diagnosed in 60 patients (9.3%); their median age was 36 years (IQR 30 - 56), and 57% were female. Fifty-two (87%) tested toxin positive. The remainder had pseudomembranous colitis at endoscopy or surgery. Forty-seven (78%) were nosocomially acquired, of which 1 was identified with NAPI. Seven (12%) CDAD patients required colectomy, and none was NAPI positive. Forty (67%) CDAD cases had recent antibiotic exposure, and 28 (47%) had previously been hospitalised. On regression analysis, previous antibiotic use (OR 2.85, 95% CI 1.61 - 5.03, p=0.0001) and previous admission (OR 1.78, 95% CI 1.02 - 3.1, p=0.04) were the only independent risk factors for CDAD. Twelve patients (20%) died, none of the deaths being related to CDAD. Of the 13 (22%) patients with community-acquired C. difficile (CA-CDAD), 10 (77%) had IBD, and 11 (85%) had had no recent antibiotic exposure. On multivariate analysis, only IBD was found to be an independent risk factor for CA-CDAD (OR 12.08; 95% CI 1.63 - 89.7, p=0.015).

Conclusion: The incidence of CDAD at GSH is lower than reported in the West. NAPI currently has little impact. One-fifth of cases were community-acquired and not associated with recent antibiotic exposure. Patients with IBD have a significantly higher risk of CA-CDAD.

MISMATCH REPAIR GENE MUTATIONS IN COLORECTAL CANCER PATIENTS IN A LOW-INCIDENCE AREA


Introduction: In a previous study we identified 206 patients with colorectal adenocarcinoma in the Northern Cape province of South Africa, diagnosed between January 2002 and February 2009. The age-standardised incidence was 4.2/100 000 per year world...
standard population. This is 10% of the rate reported in First-World countries. In high-incidence areas, the rate of abnormal mismatch repair gene expression in colorectal cancers is 5 - 10%. The aim of this study is to determine the prevalence of hMLH1- and hMSH2-deficient colorectal cancer in the Northern Cape.

Methods: Formalin-fixed paraffin blocks of tumours from 77 colorectal adenocarcinomas identified in the previous study were retrieved. Standard immunohistochemical staining methods were used to detect the expression of hMLH1 and hMSH2 gene products in the tumours.

Results: In 4 patients the immunohistochemistry staining failed, leaving 73 cases for analysis. 57 patients had evidence of both hMLH1 and hMSH2 gene product. In 10 cases hMLH1 gene product was deficient, and in 6 cases hMSH2 gene product was deficient. Overall, 16/73 (22%) of cancers were deficient for mismatch repair gene products.

Conclusion: In a low-incidence area for colorectal cancer, we found 22% of colorectal cancers to be mismatch repair gene product deficient. This is approximately four times the reported rate in high-incidence areas.

Category: Diagnostic/therapeutic

THE ROLE OF ENDOSCOPIC ULTRASOUND IN THE DIAGNOSIS OF ISOLATED ABDOMINAL LYMPHADENOPATHY IN HIV-INFECTED INDIVIDUALS

Van der Merwe S W, Corcoran C, Lameris R, Rossouw T, Slavik T

Background and study aims: Isolated abdominal lymphadenopathy poses a major diagnostic challenge, especially in HIV-infected patients. In this study we aimed to evaluate the value of endoscopic ultrasound and EUS-FNA in the diagnosis of abdominal lymphadenopathy.

Methods: HIV+ patients were screened for abdominal lymphadenopathy by echo/CT and included if no diagnosis could be made by any other diagnostic method. EUS-FNA was performed on an outpatient basis under conscious sedation. The fine-needle aspirate was collected for cytoloty, culture, flow cytometry and DNA isolation for PCR.

Results: A total of 11 HIV+ patients (mean age 35.7, 45% males) with a mean CD4+ count of 140.4 and abdominal lymphadenopathy were included in the study. Most common symptoms were fever and weight loss (both 82%). The appearance of necrotic nodes and a yellow aspirate predicted the presence of tuberculosis. 7/11 patients were positive for mycobacterium, 1/11 for lymphoma, 2 had reactive nodes and 1 had a subdiaphragmatic fluid collection. One patient was diagnosed with resistant MTB and 2 patients with M. avium intracellulare, of whom one had a MTB co-infection. Cytopathology revealed TB in 2/7 cases.

Conclusion: EUS-FNA combined with PCR in addition to standard tissue evaluation is a safe, minimally invasive and highly accurate diagnostic method in the evaluation of isolated lymphadenopathy of unknown origin in HIV-infected patients.

A PROSPECTIVE AUDIT OF DIAGNOSTIC LAPAROSCOPY IN THE DIAGNOSIS OF ABDOMINAL TUBERCULOSIS


Introduction: HIV/AIDS has resulted in a resurgence of abdominal tuberculosis in South Africa. The role of laparoscopy in making the diagnosis is undefined.

Method: All patients with clinically and radiologically suspected but histologically or microbiologically unconfirmed abdominal TB were referred to the investigating team for laparoscopy.

Results: From January 2008 to January 2010, 166 patients were referred to us. Forty-eight patients were not fit for laparoscopy. Forty-two patients required emergency laparotomy either for bowel obstruction or peritonitis. Seventy-six patients underwent diagnostic laparoscopy, and 64 of them were HIV positive. Laparoscopic findings included intra-abdominal lymphadenopathy in 53 patients, minimal ascitic fluid in 51, intra-abdominal mass in 13, and deposits on bowel wall, peritoneum or omentum in 15. In 10 patients (13.15%) an alternative diagnosis was found (appendicitis, adenocarcinoma, lymphoma). Forty-nine patients (64.47%) had positive histology for TB. In 17 patients (22.36%) histological examination revealed nonspecific inflammation and reactive lymph nodes. All but 1 of the deposits biopsied were positive for TB (14/15). The masses biopsied were positive in 85% (11/13) of cases and the lymph nodes were positive in 68% (36/53) of cases. Ascitic fluid culture was positive in 35% (8/23) cases.

Conclusion: Laparoscopy is very useful to diagnose alternative surgical pathology. Histology obtained at laparoscopy confirms the presence of TB in 65% of cases, which means all the patients with clinical and radiological evidence of TB abdomen do not actually have TB in the presence of HIV infection.

OUTCOME OF EMERGENCY LAPAROTOMY FOR ABDOMINAL TUBERCULOSIS IN A SINGLE SURGICAL UNIT

Islam J, Clarke D L, Thomson S R

Introduction: The rising incidence of HIV/AIDS has resulted in a resurgence of abdominal tuberculosis (TB) in South Africa. These often debilitated patients not infrequently present with acute complications requiring surgery.

Methods and patients: From January 2008 to April 2009, 49 patients who had positive histology for TB went for emergency laparotomy. Twenty-five were male and the mean age was 32 years. Thirty-nine were HIV positive, and HIV status of the others was unknown or negative.

Results: Only 6 patients had a prior CT abdomen. Twelve patients presented with obstruction, 9 with perforation and 28 with peritonitis without free air. Intra-operative findings were: frozen abdomen in 10 patients, bowel perforations in 13, enlarged lymph nodes and ileo-caecal mass in 19 and obstructed small bowel in 7. Eleven patients (22%) had small-bowel resection and 8 patients (16%) had right hemicolectomies. Eighteen patients (37%) ended up with stomas (16 ileostomies and 2 colostomies) and only 2 had primary anastomoses. Fourteen patients (29%) had reliaparotomies and 17 (35%) were admitted to the ICU. Twenty-three patients (47%) required blood transfusion and 15 (31%) required total parenteral nutrition. Three patients developed enterocutaneous fistula and 5 were discharged with ventral hernia. Eighteen patients died (37%), of whom only 6 had bowel resection, and 10 of them were admitted to the ICU.
ABSTRACTS

Conclusion: Emergency surgery for TB of the abdomen is associated with high morbidity and mortality with high rates of ICU admission and prolonged hospital stay, which could have been avoided by diagnostic laparoscopy.

Poster Presentations

CROHN’S DISEASE, HLA B27 AND SMALL-DUCT PSC IN BLACK SOUTH AFRICAN WOMEN: 2 CASES

Buchel O, Bosch F J, Grundling H de K

Introduction: Crohn’s disease is rare in black South Africans (0.3 per 100 000 incidence annually). HLA B27 is often associated with axial arthropathy in patients with Crohn’s disease but is similarly rare in patients from sub-Saharan Africa. Large-duct PSC, which is often associated with IBD, has been described in black people from South Africa. To our knowledge small-duct PSC has not been described in this population.

Case 1: A 26-year-old black woman with chronic diarrhoea, abdominal and back pain, was found to have Crohn’s disease involving the ascending colon and terminal ileum. No evidence of an axial arthropathy was found, and her HLA B27 was positive. Persistently elevated ALP and GGT were investigated. MRCP was normal. Liver biopsy showed small-duct PSC.

Case 2: A 44-year-old black woman with chronic diarrhoea was found to have pan-colitis, ileitis and peri-anal fistula, compatible with Crohn’s disease. HLA B27 was positive. Persistently raised ALP and GGT were noted. MRCP was normal. Liver biopsy showed small-duct PSC.

Discussion: We present 2 cases of Crohn’s disease, which are unusual as:

• Crohn’s disease is rare in black people in South Africa.
• HLA B27 is rare in black people from sub-Saharan Africa.
• Small-duct PSC has not yet been described in this population.

CHRONIC LIVER DISEASE IS A COMMON PROBLEM IN SOUTH AFRICA

Chopdat N, Ally R, Klipin M, Sparaco A

Background: Chronic liver disease is a common problem in South Africa. Liver transplantation provides a therapeutic modality for patients who have end-stage liver disease and are eligible. A lack of resources in the public sector means that few patients can be offered this modality.

Aim: The aim of this study was to review the spectrum of liver pathology from a specialised liver clinic and identify patients who would be eligible for transplantation.

Methods: From our database of patients at the liver clinic at Chris Hani Baragwanath Hospital, Soweto, patients were assessed for criteria for eligibility. The criteria included South African nationality, age less than 40, HIV negative, and a MELD score greater than 6.

Results: Over 12 months, 109 patients had been seen; 2 died, and 1 has been transplanted. Of these 108, 58 are male (55%) and 48 female (45%).

The age distribution is 6.6% under the age of 20, 37% under 40, 23% under 50 and 34% older than 50.

The majority of liver disease is cryptogenic cirrhosis (23%), then auto-immune-related diseases (16%), chronic hepatitis B (12.3%), alcohol (11.3%) and schistosomiasis (11.3%).

20 patients fulfilled the criteria (14 females, 6 males). MELD scoring revealed 5 patients with scores greater than 15 and 1 greater than 20.

Conclusion: In this small cohort of patients one-fifth were eligible for liver transplantation, suggesting a need for a liver transplant unit in the public sector.

INITIAL EXPERIENCE WITH LAPAROSCOPIC DISTAL PANCREATECTOMY

Devar J, Anderson F, Loots E, Thomson S R

Introduction: Small cystic and neuro-endocrine pancreatic tumours are ideal cases for surgeons with advanced laparoscopic skills to initiate their experience with distal pancreatic resections. We report 2 such cases.

Patients: Case A. 60-year-old woman being investigated for epigastric pain had a 5×3 cm cystic lesion in the tail of the pancreas. CT and endosonar characterisation failed to establish a diagnosis. Case B. A 29-year-old truck driver was diagnosed with a 2 cm insulinoma localised on CT and endosonar to the mid-pancreatic body.

Technique: A secure Lloyd Davies position was used. The surgeon stood between the legs. A peri-umbilical visiport was used for access and as the primary 300 optical port. 10 - 12 mm trocars were placed in the left paraxiphoid, right mid-axillary line, and left anterior axillary line. Dissection was with hook, ultrasonic and blunt dissectors. The gastroduodenal omentum was opened below the gastro-epiploic arch to expose the inferior margin of the pancreas to the left of the middle colic. The plane was extended superiorly under the pancreas, identifying and isolating the splenic vein. Dissection at the superior border of the pancreas identified and isolated the splenic artery. In case A the splenic vein was adherent to the tumour, and a distal pancreatectomy with an en bloc splenectomy was performed. Artery, vein and pancreatic parenchyma were divided with a vascular endostapler.

The spleen was mobilised by sectioning the suspending ligaments and dividing the short gastric vessels. The specimen was then removed by extending the left upper quadrant port incision. In case B the vein and artery were easily separated from the pancreas and the spleen was preserved.

Results: The hospital stays were 11 and 3 days, respectively.

There were no pancreatic complications. Histopathology of case A revealed a cystic mucinous neoplasm, and case B an insulinoma. Both were euglycaemic and well 3 months after resection.

Conclusion: Laparoscopic distal pancreatic resection is safe for selected small neoplasms of the pancreas.

SOLID PSEUDOPAPILLARY TUMOURS OF THE PANCREAS

Frost M, Bornman P C, Krige J E J, Panieri E P

Background and objective: Solid pseudopapillary tumours (SPT) of the pancreas are rare, low-grade malignant but curable tumours.
that occur almost exclusively in young women. The clinical characteristics and surgical strategy in 20 patients with SPT of the pancreas are discussed.

**Methods:** We report a retrospective review of 20 patients with SPT from patients treated over a 30-year period. Each case was evaluated with respect to age, sex, common presenting symptoms and signs, type of operation, histology and tumour markers, postoperative complications and follow-up.

**Results:** All 20 patients were female. The average age was 24.6 years (range 13 - 51). Fifteen patients presented with abdominal pain and 14 had a palpable abdominal mass on examination. Of the 20 patients, 5 had a pylorus-preserving pancreatectoduodenectomy and the remainder had local excision or required a central or distal pancreatectomy. One patient had two liver metastases that were resected in addition to the pancreatic primary lesion. One patient died of multisystem organ failure. Other significant complications included bleeding (2) requiring re-operation and intra-abdominal fluid collections requiring percutaneous drainage (3) or operation (1).

**Conclusion:** Solid pseudopapillary tumours of the pancreas should be considered in young females presenting with abdominal pain and a large pancreatic mass. Complete resection is curative in most patients and metastases are rare.

**VATS AT SEBOKENG HOSPITAL: INITIAL EXPERIENCE**

**Isakov R, Koto M Z**

**Introduction:** VATS has been used in a variety of settings, with minimal morbidity and mortality. We document our initial experience at Sebokeng Hospital.

**Method:** Over the period 1/5/2006 to 13/5/2010, we collected records of patients who had undergone VATS at Sebokeng Hospital and Clinix Private Hospital. Demographics, clinical indication, operative findings, outcome and complications were looked at. The procedure was done under general anaesthetic, using single-lung ventilation (except 8-month-old patients).

**Results:** Over a period of 48 months 19 male and 6 female patients underwent VATS. The average age was 36 years (range 8 months - 69 years).

Indications for VATS included:

- Trauma: non-resolving haemo/pneumothorax, empyema, foreign body retention
- Pleural and lung biopsy
- Pneumonic complication
- Mediastinal mass
- Cervical sympathectomy for hyperhidrosis.

Complications included 1 patient who was converted to open thoracotomy because of extensive adhesions and 2 patients with incomplete lung expansion. One patient required transfusion; recovery was otherwise uneventful. There were no deaths.

**Conclusion:** VATS is a viable and safe option for clotted haemothorax and decortications as well as many other indications. Early intervention is advised to avoid complications.
and procedural success rate have decreased. More detailed analysis of case mix and the effect of a well-developed interventional radiological service on overall therapeutic success is required.

BILIARY ASCARIS CAUSING ACUTE PANCREATEITIS – A CASE REPORT

Naidoo V G

Introduction: Pancreatitis is a rare but well-documented complication of *Ascaris lumbricoides* infestation. Diagnostic and therapeutic strategies to manage biliary ascaris are not well defined.

Case presentation: A 17-year-old man was referred to our unit following two episodes of pancreatitis without discernable cause. The liver enzymes were normal and a transabdominal ultrasound suggested a possible common bile duct (CBD) lesion. Endosonar revealed a hyperechoic mass within the CBD without accompanying acoustic shadow. Biliary ascaris was considered the most likely diagnosis. Endoscopic retrograde cholangiography confirmed a linear filling defect in the CBD and following sphincterotomy a 30 cm worm was extracted per os using a combination of an extraction balloon and dormia basket. The patient was subsequently treated with albendazole and made an uneventful recovery. No further episodes of pancreatitis symptoms were reported at review 1 month later.

Discussion: Transabdominal ultrasound diagnosis of biliary ascaris requires a high level of expertise. Endosonar provides excellent definition of the CBD and may prove a useful additional diagnostic tool in such cases prior to endoscopic therapy. Most cases can be managed medically, with endoscopic therapy or surgery being restricted to specific clinical situations. The best clinical practice method of endoscopic worm extraction has not been defined, but avoidance of sphincterotomy is recommended owing to concern about facilitating worm migration in the event of future re-infestation.

Conclusion: Ascaris infestation is endemic in South Africa. This case report highlights an important complication that may be encountered by gastro-enterologists and surgeons. Rapid diagnosis using available tools, selecting an appropriate management strategy and good follow-up usually results in a satisfactory clinical outcome.

PPARγ IS SIGNIFICANTLY REDUCED IN COLORECTAL CANCER COMPARED WITH INFLAMMATORY BOWEL DISEASE AND IRRITABLE BOWEL SYNDROME

M Ngaira, E Fredericks, E Shivji, S Williams, G Dealtry, S Roux

Background: Colorectal cancer is the 4th most common cause of cancer death. The early stages of carcinogenesis are poorly understood. Identification of appropriate target genes and their downstream effects is important in the early detection of colon carcinogenesis and to develop appropriate intervention at the molecular level. Variation in mRNA in tissue biopsies indicating changes in gene expression can be analysed by quantitative reverse transcription PCR (qRT-PCR). PPARγ and SREBP are important transcription factors involved in the regulation of inflammation and cellular differentiation.

Aim: To compare expression of PPARγ and SREBP in colon biopsies from screening colonoscopy, irritable bowel syndrome (IBS), inflammatory bowel disease (IBD) and CRC.

Methods: mRNA was extracted from colon biopsies, stored in RNALater (Ambion, USA) and reverse transcribed to cDNA. The relative expression patterns of PPARγ and SREBP were determined using gene-specific primers and changes in specific gene expression between samples were normalised with reference to two sets of Alu repeats and one stably expressed reference gene.

Results: Expression of PPARγ in 80 biopsy samples showed clear differences between normal patients and those with colorectal pathology. Relative expression of PPARγ was significantly reduced in samples from patients with CRC (5-fold) compared with patients in the normal screening colonoscopy group (p<0.01). Furthermore, relative expression of PPARγ in biopsies from patients with CRC was reduced 3-fold compared with all other patients (IBD and IBS) (p<0.005). In contrast, no significant change in the relative expression of SREBP was found.

Conclusion: Expression of PPARγ was downregulated in all colon pathologies and further downregulated in colon cancer, whereas expression of SREBP, an upstream transcription factor, remained unchanged. This confirms the central role of PPARγ in colon carcinogenesis and indicates regulation by an SREBP-independent mechanism.

AIDS PERINEUM

Tun M

Aim: To study perineal manifestations of AIDS.

Method: The study period was from 2000 to 2010. Patients from Lesedi Hospital were recruited. Patients who had AIDS and were treated by the author were included. All received standard treatment for AIDS.

Results: Fifty-eight patients (28 males and 30 females), mean age 30.5 years (range 22 - 44), were included. Follow-up ranged from 2 weeks to 6 years. Symptoms were proctalgia (35), soiling (50), bleeding (6) and lumps (6). Every patient underwent EAU of the perineum. The findings were multiple fistulas (35), peri-anal abscesses (7), anal ulcers (27), prolapsed haemorrhoids (5) and poor anal tone (49). The treatments were local steroid injection (4), colostomy (2), fistulotomy (10), I&d (4), HAART (50) and biopsy (48). Thirty-eight patients died during follow-up. Biopsies revealed mycobacterium (6), CMV (1) and nonspecific (41). Fifteen had proctalgia improved (none received local steroid injection), 12 had soiling improved, 17 had sepsis healed and 8 had persistent soiling (7 had fistulotomy with 1 non-healing wound) in the survivors. All patients with CMV and mycobacterium infections died.

Conclusion: Perineal manifestations reflect AIDS and urgent need for HAART. Concomitant CMV and mycobacterium infections predict poor outcome. Only patients who responded well to HAART had a good outcome.
Prevalence of Bacterial Infection in Non-Cirrhotic Variceal Bleeding Patients at Maputo Central Hospital, Mozambique

Van der Merwe S, Cunha L, Modocoar P

Introduction: Bacterial translocation and sepsis often occur in chronic liver disease, leading to decompensation of liver function. In patients with liver cirrhosis presenting with variceal bleeding, bacterial infections are particularly common. In fact 50% of CLD with variceal bleeding will have culture-positive infections that may directly impact on the outcome of therapy and mortality. This has led to the Baveno consensus recommending the use of antibiotics in the management of variceal bleeding. However, the prevalence and importance of bacterial infections in non-cirrhotic portal hypertension has not been studied.

Aim: We studied the prevalence of bacterial infections in consecutive non-cirrhotic variceal bleeding patients.

Patients and methods: Patients with variceal bleeding were included in the study. At presentation blood and urine cultures were obtained, and the white cell count and CRP level were measured. Non-cirrhotic portal hypertension was confirmed by calculating the Child-Pugh score and excluding liver cirrhosis by means of sonography and appropriate serological tests.

Results: 31 patients were included in the study, of whom 71% (22/31) were male. Blood and urine cultures were positive in 29% (9/31) and 10% (3/31), respectively. Only 1 patient died during the hospital admission.

Discussion: The importance of bacterial sepsis in variceal bleeding due to non-cirrhotic portal hypertension remains unknown. Our study showed that culture-positive bacterial infections occurred in 29% of patients. This is substantially lower than described for cirrhotic liver disease. However, it still suggests that bacterial infections may affect the outcome of these patients, requiring the use of prophylactic antibiotic therapy in the management of variceal bleeding.