

GASTRO RESEARCH

Gastroenterology elsewhere

Korman J D, Volenberg I, Balko J, *et al.* and the Pediatric and Adult Acute Liver Failure Study Groups. **Screening for Wilson disease in acute liver failure: a comparison of currently available diagnostic tests.** *Hepatology* 2008;48:1167–74

Wilson disease (WD) is the etiology in $\approx 5\%$ of acute liver failure (ALF) patients. Almost all patients with WD presenting with ALF die rapidly without urgent transplantation. The predictive value of currently available serum markers for diagnosis of WD is suboptimal in the setting of ALF.

The authors evaluated investigations of 140 consecutive patients with encephalopathy and INR >1.5 from the ALF registry. Parameters in 16 patients with ALF due to WD were compared with 124 patients with ALF due to other causes (acetaminophen hepatotoxicity 37%, drug toxicity 13%); 17 patients with stable WD were studied as controls. The values of biochemical tests in WD and other causes of ALF were: ALT (24.5 vs 1830 IU/L; $p<0.01$), AST (185 vs 1337 IU/L; $p<0.01$), total bilirubin (42.1 vs 7.3 mg/dL; $p<0.01$), hemoglobin (7.0 vs 11.6 g/dL; $p<0.01$), serum ceruloplasmin by oxidase method (22.7 vs 30.9 mg/dL; $p=0.02$), serum ceruloplasmin by nephelometry (18.7 vs 22.9 mg/dL; $p=0.2$), copper (272 vs 91.5 $\mu\text{g/dL}$, $p<0.01$), alkaline phosphatase (ALP) to bilirubin ratio (0.5 vs 20.1, $p<0.01$) and AST:ALT ratio (7.5 vs 1.0). ALP to bilirubin ratio <4 had a sensitivity of 94%, specificity of 96%, and a likelihood ratio of 23, and AST:ALT ratio >2.2 had a likelihood ratio of 7 for diagnosing fulminant WD. Combining the tests provided a diagnostic sensitivity and specificity of 100%. Serum ceruloplasmin <20 mg/dL by the oxidase method had likelihood ratio of 1. Serum free copper levels >200 $\mu\text{g/dL}$ had a sensitivity of 75%, specificity of 96% and likelihood ratio of 17. Hemoglobin <10 gm/dL had a likelihood ratio of 4. Median MELD score for WD patients was 40 while that for non-WD patients was 34 ($p<0.01$).

The authors concluded that ALP, bilirubin and aminotransferases provide the most rapid and accurate method for diagnosis of ALF due to WD while conventional tests like serum ceruloplasmin are less sensitive and specific.

Villoria P, Garcia X, Calvet J, P, Vergara G M. **Meta-analysis: high-dose proton pump inhibitors vs. standard dose in triple therapy for *Helicobacter pylori* eradication.** *Aliment Pharmacol Ther* 2008;28:868–77

Acid inhibition is a key component of *Helicobacter pylori*-eradication therapy (HPET). Increasing the dose of proton pump inhibitors (PPI) is known to increase cure rates.

The authors carried out meta analysis of studies comparing efficacy of HPET containing high-dose PPI (omeprazole 40 mg, esomeprazole 40 mg) and standard dose (omeprazole 20 mg, pantoprazole 40 mg, rabeprazole 20 mg and esomeprazole 20 mg) in twice a day regimens along with clarithromycin and either metronidazole or amoxicillin for at least 7 days. *H. pylori* eradication was confirmed by urea breath test and/or biopsy. Six studies, with 1703 patients were included in the meta-analysis. On intention-to-treat analysis, cure rates of high-dose PPI were 583/711 (82%, 95% CI: 78–84) vs. 734/992 (74%) with the standard dose (95% CI: 4–11; NNT 15, 95% CI: 8–135). RR for curing the infection with the higher doses was 1.09 (95% CI: 1.01–1.17). After exclusion of an outlier study, RR of cure rate fell to 1.06 (95% CI: 1.00–1.12) and significance remained borderline ($p = 0.04$). On per protocol analysis, cure rates were 582/655 (88.9%, 95% CI: 86–91) in the high-dose group vs. 730/891 (81.9%, 95% CI: 79–84) in the low dose (95% CI: 3–10; NNT 20, 95% CI: 12–122).

Authors concluded that high-dose PPI seems more effective than standard-dose for curing *H. pylori* infection in 7-day triple therapy.

Wang P, Li Z-S, Liu F, *et al.* **Risk factors for ERCP-related complications: a prospective multicenter study.** *Am J Gastroenterol* doi: 10.1038/ajg.2008.5

Many prospective multicenter studies have evaluated the patient- and procedure-related risk factors for ERCP-related complications. Transient hyperamylasemia, which is a common manifestation of injury to the pancreas and often not associated with clinical signs, is not usually recognized in previous studies. The contribution of pancreatic deep wire pass and transpancreatic precut to ERCP-related complications is not known.

This prospective, multicenter study conducted at 14 centers in China, was planned to investigate the potential risk factors for endoscopic retrograde cholangiopancreatography (ERCP) complications and to identify whether the risk factors are different for pancreatitis and asymptomatic hyperamylasemia. A total of 3,178 consecutive ERCP procedures were performed on 2,691 patients in 12 months. The complications after the patients' first procedure were evaluated and the risk factors identified using a multivariate analysis.

Complications were seen in 213 (7.92%) patients, pancreatitis in 116 (4.31%), and asymptomatic hyperamylasemia in 396 (14.72%). In the multivariate analysis, female gender (adjusted OR 1.52), periampullary diverticulum (OR 2.02), cannulation time >10 min (OR 1.51), ≥ 1 pancre-

atic deep wire pass (OR 1.80), and needle-knife precut (OR 2.70) were significant risk factors for overall complications. Female gender (OR 1.84), age ≤ 60 year (OR 1.59), cannulation time >10 min (OR 1.76), ≥ 1 pancreatic deep wire pass (OR 2.77), and needle-knife precut (OR: 4.34) were significant risk factors for pancreatitis. Cannulation time >10 min (OR: 1.96), ≥ 1 pancreatic deep wire pass (OR: 2.24), needle-knife precut (OR: 2.34), and major papilla pancre-

atic sphincterotomy (OR: 1.71) were significant risk factors for asymptomatic hyperamylasemia.

Thus, patient-related factors are as important as procedure-related factors in determining high-risk predictors for post-ERCP overall complications and pancreatitis. The risk factors for asymptomatic hyperamylasemia are mostly procedure related, and may be different from those of pancreatitis.

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Gastroenterology India

Bhardwaj P, Garg PK, Maulik SK, Saraya A, Tandon RK, Acharya SK (All India Institute of Medical Sciences, New Delhi). **A randomized controlled trial of antioxidant supplementation for pain relief in patients with chronic pancreatitis.** *Gastroenterology* doi:10.1053/j.gastro.2008.09.028.

Chronic pancreatitis (CP) is a progressive inflammatory disease of the pancreas resulting in slow destruction of pancreatic parenchyma and subsequent fibrosis. Increased oxidative stress has been found in patients with alcoholic and idiopathic chronic pancreatitis. Some benefit of antioxidants supplementation has been found in patients with CP. This randomized controlled trial studied the role of antioxidant supplementation for relief from pain and attenuation of oxidative stress in patients with CP.

Consecutive patients with CP (35 alcoholic, and 92 with idiopathic CP) were randomized to placebo ($n = 56$) or antioxidants ($n = 71$) for 6 months. The antioxidant supplementation included daily doses of 600 μg organic selenium, 0.54 g ascorbic acid, 9000 IU β -carotene, 270 IU α -tocopherol and 2 g methionine (*Betamore G*, Osper Pharmaceutics, India). The markers of oxidative stress (serum superoxide dismutase [SOD] and thiobarbituric acid reactive substances [TBARS]) and antioxidant status (vitamins A, C, and E; total antioxidant capacity [measured as ferric reducing ability of plasma; FRAP], total glutathione [T-GSH], and erythrocyte SOD [e-SOD]) were estimated both before and after treatment. The primary outcome measure was pain relief, and secondary outcome measures were analgesic requirements, hospitalization, and markers of oxidative stress. After 6 months, the reduction in the number of painful days per month was higher in the antioxidant group compared with placebo (7.4 vs 3.2, respectively; $p < 0.001$; 95% CI, 2.07, 6.23). The reduction in the number of analgesic tablets per month was also higher in the antioxidant group (10.5 vs 4.4, respectively; $p = 0.001$; 95% CI, 2.65, 9.65). The requirement of parenteral analgesic injections, which was comparable at baseline, also decreased significantly at 6 months in the antioxidants group ($p = 0.026$). Also, 32% of patients who received antioxidants became pain free as compared to 13% of those who received placebo ($p = 0.009$). At six

months, TBARS decreased ($p = 0.001$), FRAP increased ($p = 0.038$), and SOD decreased ($p < 0.001$) in the antioxidant group as compared with that in the placebo group. The reduction in the level of TBARS and increase in FRAP were higher in the antioxidant group compared with the placebo group.

This randomized trial shows that antioxidant supplementation is effective in relieving pain and reducing levels of oxidative stress in patients with CP.

Bhatia V, Singhal A, Panda SK, Acharya SK (All India Institute of Medical Sciences, New Delhi). **A 20-year single-center experience with acute liver failure during pregnancy: is the prognosis really worse?** *Hepatology* 2008;48:1577–85.

The causes of acute liver failure (ALF) differ across the globe. In India and many other developing countries, HEV is the most common cause of endemic and epidemic acute hepatitis. Pregnant patients with ALF are believed to have a worse outcome than non-pregnant women and men with ALF. However, it is still not clear whether liver failure during pregnancy has a worse prognosis.

The current retrospective study assessed the outcome of 1015 consecutive patients with ALF in the reproductive age group admitted from January 1986 to December 2006. In this cohort, 249 (38.5%) women were pregnant, 341 were nonpregnant women and girls, and 425 were men and boys, aged 15 to 45 years. Overall, 575 (56.7%) patients died, with admission to death interval of mean 5.1 (SD 4.2) days. The mortality rate among pregnant women and girls was 53.8% (134 of 249), and was similar to that among age-matched nonpregnant women and girls (57.2%; 195 of 341) and among men and boys (57.9%; 246 of 425). The clinical and biochemical features, disease severity, and complications were also similar in the three groups. A higher proportion of ALF was attributable to hepatitis E virus (HEV) among women and girls who were pregnant (145/244; 59.4%), as compared with both nonpregnant women and girls (100/329; 30.4%), and men and boys (97/420; 23.1%; $p < 0.001$). Mortality in HEV-ALF and non-HEV-ALF patients in pregnant women and girls was similar (74/145 [51%] vs

52/95 [54.7%], respectively). The outcome of pregnant ALF patients was not related to the trimester of the pregnancy. The gestational periods of the 115 pregnant survivors and 134 pregnant nonsurvivors were 26.2 (6.3) weeks and 27.1 (6.0) weeks, respectively. The mortality of non-HEV-related ALF among the pregnant women and girls (54.7%), age-matched nonpregnant women and girls (61.7%), and men and boys (62.8%) were also similar. Presence of cerebral edema and higher grade of encephalopathy at admission, longer icterus-to-encephalopathy interval, higher bilirubin and creatinine levels, prothrombin time prolongation, and HEV as etiology for ALF significantly influenced outcome among women and girls. Pregnancy status did not confer increased mortality risk for women and girls (odds ratio for mortality, 0.87; 95% CI, 0.62–1.23).

Thus, the mortality of pregnant women with ALF is similar to that of age-matched nonpregnant women and girls and men and boys with ALF. Pregnancy *per se* should not be regarded as a poor prognostic factor for a patient with ALF.

Balamurugan R, Janardhan HP, George S, Chittaranjan SP, Ramakrishna BS. **Bacterial succession in the colon during childhood and adolescence: molecular studies in a southern Indian village.** *Am J Clin Nutr* 2008;88:1643–7.

Gut flora has been implicated in the pathogenesis of many GI diseases such as inflammatory bowel diseases, irritable bowel syndrome, and necrotizing enterocolitis. The gut of the newborn is sterile at birth. The bacterial flora is established at or shortly after birth by bacteria in the immediate environment. It is believed that once the flora is established in the early years, it generally continues to exist unchanged through life. To clearly understand the basis of this relation, and before introducing interventions such as probiotics to promote health, it is important to characterize the bacterial composition of the gut in a population of healthy persons. There is a lack of data on the succession of bacterial flora from childhood to adolescence in Indian healthy people.

The present study was done to determine whether the bacterial flora of the colon undergoes further changes (succession) during childhood and adolescence. In a cross-sectional study, the authors examined fecal samples from 130 healthy children and adolescents in the age group 2–17 years, and from 30 healthy adults (median age: 42 years) residing in a single village in southern India. Fecal DNA was subjected to 16S rDNA-targeted real-time polymerase chain reaction to determine the relative predominance of *Bifidobacterium* genus, *Bacteroides-Prevotella-Porphyromonas* group, *Lactobacillus acidophilus* group, *Eubacterium rectale*, and *Faecalibacterium prausnitzii*. *Bifidobacterium* species and *Bacteroides-Prevotella* group were dominant fecal bacteria overall. Age-related differences were found amongst the relative distribution of various bacteria. The *Bifidobacterium* genus was very prominent at ages 2–3 years and showed a steep decline in adults ($p < 0.0001$). The *Bacteroides-Prevotella-Porphyromonas* group of bacteria was a major constituent of fecal bacterial flora in older children and adults; they were relatively lower in number at ages 2–3 and gradually increased in number to peak to adult levels by the age of 17 years.

There was a rapid decline in *Lactobacillus* in the preschool children (3–4 log reduction) so that by the time a child reached school-going age, the number of bacteria of the *Lactobacillus* group were extremely low. Changes during adolescence included an increase in *E. rectale* and *F. prausnitzii*. There was an increase in *Bacteroides* during late adolescence and in adults ($p = 0.0040$). *E. rectale* and *F. prausnitzii* along with *Bacteroides*, are main producers of short-chain fatty acids from fermentation of unabsorbed carbohydrates and thus important to colonic physiology.

In conclusion, changes occur in the composition of the fecal anaerobic bacterial flora through childhood and adolescence, and suggest that the bacterial flora of the gut is engaged in an ongoing process of change and bacterial succession with ageing.