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## 13<sup>th</sup> Euro-Global Gastroenterology Conference August 20-21, 2018 | Rome, Italy

# Posters

# Gastro Congress 2018

# 13th Euro-Global Gastroenterology Conference

August 20-21, 2018 | Rome, Italy

## Epidemiological and Clinical evaluation of Hepatitis B, Hepatitis C, and delta Hepatitis viruses in Tajikistan

#### Dustov Abdusamad

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Nhronic HBV and/or HCV infection can progress to liver cirrhosis and hepatocellular carcinoma (HCC) [1-4]. Among 124 hepatitis patients, 84 (67.7%) were assigned into chronic hepatitis (group 1) and 40 (32.2%) into liver cirrhosis/HCC (group 2). There was no significant difference in age between both groups. The HCV was positive in only 4 of the 15 cases, suggesting that HCV RNA was degraded in these samples, while remaining 11 cases had resolved acute HCV infection. HCV infection was found to be high in both groups (group 1 = 47.6% and group 2 = 42.5%). HCV RNA was detected in 91% of cases (100% in group 1 and 70.5% in group 2). Anti-HBc was found to be high in both groups (94% and 87.5%, respectively). Although Seroprevalence of anti-HBs was very low (12.1%) in the studied population but significantly high in group 1 (16.6%) than group 2 (P = 0.0356).. The Seroprevalence of HBsAg was equally high in both groups, that is, group 1 = 40.4% and group 2 = 42.5%, whereas DNA positivity was 70.5% and 76.4%, respectively. Overall anti-HDV Seroprevalence was 23.5%, 12 out of 51 HBsAg positive cases, relatively higher in group 2 (35.2%) compared to group 1 (17.6%) P = 0.1990. HDV viremia was detected in 83.3% of cases (100% in group 1 and 66.6% in group 2). HCV genotyping was determined as HCV genotype 2c (HCV/2c) in E1 region. A total of 7.6% of cases were un-typeable by one of either method. Overall, HCV/1b was a predominant genotype (84.6%) in Tajikistan, followed by HCV/3a (7.6%), 2a (5.7%), and 2c (1.9%). HBV genotype D (HBV/D) was the predominant genotype (94.1%) in both groups, that is, group 1 = 97% and group 2 = 88.2%, followed by genotype A (2.9% and 11.7%, respectively). HBV genotypes were determined in 45 (88%) of 51 HBsAg-positive. The full genome analysis revealed that of the four HBV/D strains, two belonged to sub genotype D1, and the remaining two to sub genotype D2. All three HBV/A strains in this study were belonged to sub genotype Ae. The results of the phylogenetic genotyping were all concordant with EIA-genotyping results (Fig.).

#### **Recent Publications:**

- 1. Bakarey AS, Olaniyan OD.Hepatitis B virus infection among asymptomatic residents of low income community in Ibadan, Southwest, Nigeria.J Immunoassay Immunochem. 2018 May 14:1-13.
- 2. Casey JL, Niro GA, Engle RE, Vega A, Gomez H, McCarthy M, Watts DM, Hyams KC, Gerin JL. 1996. Hepatitis B virus (HBV)/hepatitis D virus (HDV) coinfection in outbreaks of acute hepatitis in the Peruvian Amazon basin: The roles of HDV genotype III and HBV genotype F. J Infect Dis 174:920-926.
- 3. Luma HN, Eloumou SA, Ekaney DS, Lekpa FK, Donfack-Sontsa O, Ngahane BH, Mapoure YN. Sero-prevalence and Correlates of Hepatitis B and C Co-infection Among HIV-infected Individuals in Two Regional Hospitals in Cameroon.Open AIDS J. 2016 Nov 3;10:199-208.
- 4. Farooq A, Waheed U, Zaheer HA, Aldakheel F, Alduraywish S, Arshad M. Detection of HBsAg mutants in the blood donor population of Pakistan.PLoS One. 2017 Nov 22;12(11).
- 5. Tang LSY, Covert E, Wilson E, Kottilil S. Chronic Hepatitis B Infection: A Review. JAMA. 2018 May 1;319(17): Review.

#### Biography

Dustov Abdusamad is of the age 64 years from Bangladesh. He is working as Head of the Department of Virology in the Institute of Gastroenterology of Republic of Tajikistan. He is greatly interested in research works on Viruses. He participated in many international conferences. He has more than 20 publications.

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### Relationship between long term use of PPIs and vitamin B12 level

Rami George Maalouf, Hani Waked and Elias Makhoul Holy Spirit University of Kaslik, Lebanon

**Background:** Gastric acid inhibitors may decrease vitamin B12 absorption and thus lead to vitamin B12 deficiency. PPIs (Proton pump inhibitors) are often overused in the Lebanese population.

**Objectives:** The objective of this study is to evaluate the relationship between the use of proton pump inhibitors and vitamin B12 deficiency in a Lebanese population.

**Methods:** A retrospective case-control study based on a sample of 210 outpatients from the Lebanese community was performed. We compared 70 patients who were originally diagnosed with vitamin B12 deficiency between May 2016 and May 2017 with 140 patients without vitamin B12 deficiency.

**Results:** After comparing the two groups, cases and controls, that were matched by age and gender, we found that there was a significant P value of 0.0001, indicating that the number of long-term PPI users (equal or more than 2 years) have a higher proportion among the cases (vitamin B12 deficiency) than among the controls (no vitamin B12 deficiency). In addition, we found that the P value is more significant in the "only women" group (P=0.004), but P values concerning age groups are not coherent.

**Conclusions:** We conclude that a significant association between long-term proton pump inhibitors use and vitamin B12 deficiency in a Lebanese population exists, which is stronger among women but unclear concerning the age groups.

#### Biography

Rami George Maalouf is graduated from Holy Spirit University of Kaslik in 2018. Now he is in PGY 1 Gastroenterology. He is very much interested on IBD research works and has publications on IBD researches. Currently he is working on IBD.

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## Seroprevalence and risk factors of Hepatitis delta virus in chronic Hepatitis B virus infection in Tajikistan

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Hepatitis delta virus (HDV) infection results in more severe and even fulminant form of hepatitis B in co-infected cases. This study was designed to estimate the prevalence of anti-HDV positivity and the associated risk factors in patients with chronic hepatitis B virus infection in Tajikistan. In this cross-sectional study a total of 440 consecutive patients with chronic hepatitis B virus (HBV) infection attending the Institute Gastroenterology of the Ministry of Health, Republic of Tajikistan clinic from 2014 to 2017 were included. We performed test for HDV serum marker, using commercially available enzyme-linked immunosorbent assay kit. Patients were split into two groups according to their HDV antibody status as HDV positive or negative. The collected data were coded, and the statistical analyses were conducted. 440 patients with various forms of chronic HBV-related liver diseases enrolled in the study. 200 (45.5%) patients were carrier for HBV. 196 (44.5%) patients had chronic active hepatitis and 44 (10%) patients suffered from cirrhosis. Anti-HDV was demonstrated in 75 patients (17%). The prevalence of HDV was 7%, 16.3% and 65.9% in carriers, patients with chronic active hepatitis and cirrhosis, respectively. HDV infection is still an important public health problem in Tajikistan and appears a major cause of progression of liver disease induced by HBV.

#### **Recent Publications:**

- 1. Husa P, Linhartova A, Nemecek V, Husova L. Hepatitis D. Acta Virol. 2005;49(4):219-25.
- 2. Govindarajan S, Chin KP, Redeker AG, Peters RL. Fulminant B viral hepatitis: role of delta agent. Gastroenterology. 1984;86(6):1417-20.
- 3. Rizzetto M, Canese MG, Aricò S, Crivelli O, Trepo C,Bonino F, Verme G. Immunofluorescence detection ofnew antigen-antibody system (delta/anti-delta) associatedto hepatitis B virus in liver and in serum of HBsAg carriers. Gut. 1977;18(12):997-1003.
- 4. Hughes SA, Wedemeyer H, Harrison PM. Hepatitis delta virus. Lancet 2011Apr19
- 5. Celen MK, Ayaz C, Hosoglu S, Geyik MF, Ulug M. Antihepatitis delta virus seroprevalence and risk factors in patients with hepatitis B in Southeast Turkey. Saudi Med J 2006; Vol. 27 (5): 617-620.

#### Biography

Ramazanova Zamira is of age 63 years from Institute of Gastroenterology of the Republic of Tajikistan. She works at the Department of virology, Institute of Gastroenterology of the Republic of Tajikistan. She has published more than 30 papers in reputed journals.

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#### A real life experience of IBD patients treated with biologic treatment vs immunomodulators

Rami George Maalouf, Hani Waked, Charbel Yazbeck, Caline Azzi, Michel Dagher, Souheil Hallit and Yara Assaf Holy Spirit University of Kaslik, Lebanon

Treatments and therapeutic approaches in IBD are constantly evolving. The newly emerged biologic treatments are one such evolving approach, with much ongoing studies to determine the outcomes safety and side effects, in comparison to the older immunosuppressive treatment regimens. In this research, a retrospective analysis was conducted on 112 patients with IBD, retrieved from a single center in Lebanon, with the aim of evaluating the outcomes of biologic, immunosuppressive, or combination of both drug classes, over one another, in the treatment of patients with IBD in the real life experience. Patient treated with Azathioprine were 58%, patients receiving Infliximab were 13%, 20% received Adalimumab, and only 8.9% of patients received a combination of Azathioprine and Adalimumab. Overall response rates to treatment were high (92.9%), while non-responders were 7.1%. As for flare up rates, it was observed that 32.1% of patients had flare ups during treatment, while the majority (61.6%) did not. Less flare up and side effect rates were noted among patients treated with biologic treatment. In addition, the results showed that biologic drugs are superior in achieving a higher response rate compared to immunosuppressive treatment. This result was significant to the 95% confidence interval.

#### **Biography**

Rami George Maalouf is graduated from Holy Spirit University of Kaslik in 2018. Now he is in PGY 1 Gastroenterology. He is very much interested on IBD research works and has publications on IBD researches. Currently he is working on IBD.

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### Congenital diaphragmatic hernia & some complications

Mykhailo Bilousov Danylo Halytsky Lviv National Medical University, Ukraine

**Statement of the Problem:** A 22-year-old nulliparous woman was announced at 22 weeks' gestation that her foetal had a leftsided congenital diaphragmatic hernia (CDH): stomach, loops of bowel and a major portion of the liver herniated into the chest, squashing the lung (lung hypoplasia) and pushing the heart over to right side of the chest.

**Purpose:** The purpose of this study is to describe in retrospection the case of successful surgical repair carried out at The Children's Memorial Health Institute (Warsaw, Poland).

**Methodology & Theoretical Orientation:** The probability of cardiovascular, digestive, neurologic or skeletal congenital malformation, and persistent pulmonary hypertension as serious consequences was not excluded. There was a possibility to have gastroesophageal reflux (GER), one of the major sequelae in infants who survive CDH repair. CDH might be a source of feeding problems, failure to thrive, esophagitis and respiratory problems. Foetal karyotype was normal. The mother decided to give birth to her son despite doctors advising her to terminate the pregnancy (there was no chance to survive in Ukraine). Mother made every effort to find a clinic abroad that would agree to do Caesarean and a successful newborn operation.

**Findings:** The main conditions for A Dubravsky's survival were: a great mother's love, prenatal diagnosis of CDH, formulation of management strategy based on the prognostic elements, skilful Caesarean section, postnatal care of the newborn, stabilization, prompt transportation, emergent surgery performed by great Polish specialists and compensatory growth of the lungs.

**Conclusions & Significance:** The outcome was favourable with a 14-year follow-up. Epigastric pain, chronic cough and recurrent bronchitis are reported. Thoracic deformities are observed. At the time of writing the child was growing satisfactory and there were no apparent digestive disorders. The chance of the next baby having CDH was very small, so his sister was born in 2012 without CDH.

#### **Recent Publications:**

- 1. Puligandla P and Skarsgard E D (2016) The Canadian pediatric surgery network congenital diaphragmatic hernia evidence review project: developing national guidelines for care. Paediatrics & Child Health. 21(4):183-186.
- 2. Lally K P and Engle W (2008) Postdischarge follow-up of infants with congenital diaphragmatic hernia. Pediatrics. 121(3):627-632.
- 3. Peetsold M G et al. (2009) The long-term follow-up of patients with a congenital diaphragmatic hernia: a broad spectrum of morbidity. Ped. Surg. Int. 25(1):1-17.
- 4. Jaillard S M et al. (2003) Outcome at 2 years of infants with congenital diaphragmatic hernia: a population based study. Ann. Thorac. Surg. 75(1):250-256
- 5. Clark R H et al. (1998) Current surgical management of congenital diaphragmatic hernia: a report from the congenital diaphragmatic hernia study group. J. Pediatr. Surg. 33(7):1004-1009.

#### Biography

Mykhailo Bilousov is currently a 4<sup>th</sup> year student of Danylo Halytsky Lviv National Medical University. He has given a retrospective analysis of the case of successful surgical repair of congenital diaphragmatic hernia. The abstract is aimed to attract attention of the scientists all over the world to the CDH problem in order to find new ways of its treatment. It showed the great interest of the author in improving the health and well-being of the population. He has focused on achieving positive results in medicine and gaining improvement in the methods of treatment of severe and rare pathologies.

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## Ceramide as a mark of severity and activity of diabetes mellitus type 2 and nonalcoholic fatty liver disease

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**Introduction:** Sphingolipids are biological active components of all cell membrane. They play a great role in cell interconnections and take part in such process as a proliferation, maturation and cell apoptosis. Ceramide deserve special an attention, because they could be precursors of apoptosis and lead to development of diabetes mellitus type 2 (DM type 2) and nonalcoholic fatty liver disease (NAFLD).

**Objectives:** The objective of this study is to investigate dependence between ceramide levels in plasma, level of insulin and HOMA (homeostatic model assessment) indices in patients with DM type 2 and activity of AST(aspartate transaminase), ALT (alanine transaminase) in patients with NAFLD.

**Materials & Methods:** We performed researches in three groups. The total number of patients was 60 (n=60). Two of them consisted of patients with DM type 2 and NAFLD (n=20, n=20 respectively) and the third one was healthy persons. The level of insulin, HOMA indices and activity of AST and ALT were assessed by using common biochemical blood analyses. Plasma ceramides (C14:0, C16:0, C18:0, C18:1, C20:0, C24:0 and C24:1) were quantified using electrospray ionization tandem mass spectrometry after separation with HPLC.

**Results:** As result of researches, we got data that show high levels of ceramide in the first and second group comparing with healthy persons. This result is tightly correlated with the high level of insulin, HOMA indices and activity of AST and ALT in patients with DM type 2 and NAFLD respectively.

**Conclusions:** During our researches, we found out dependence between high ceramide levels with severity of DM type 2 and activity rate of NAFLD. So, further investigation of ceramide is needed for taking them as parameters for prognosis DM type 2 severity or as development NAFLD complications such as nonalcoholic steatohepatitis.

#### Biography

Leonid Pavlovskyi, Doctor graduated from National Medical University. She is currently working in Gastroenterology Department in one of the central hospital. She also works as an Assistant of Internal Medicine Department of National Medical University.

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Hepatotoxicity and related risk factors of severe hepatotoxicity among HIV-1 infected individuals initiated on highly active antiretroviral therapy (HAART) in Cameroon

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<sup>2</sup>Kenyatta University, Kenya

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<sup>4</sup>University of Yaoundé I, Cameroon

<sup>5</sup>Mbingo Baptist Hospital – CBCHS, Cameroon

**Aims/Purpose:** Hepatotoxicity due to highly active antiretroviral therapy (HAART) has gained prominent attention since it can be affected by many factors. The aim of this study was to determine the prevalence of hepatotoxicity and related risk factors of severe hepatotoxicity following HAART initiation.

**Methods:** One hundred naive HIV-1 patients were recruited and followed up for 24 weeks. They were placed on either Tenofovir (TDF)+Lamivudine (3TC)+Efavirenz(EFV) or Zidovudine (AZT)+Lamivudine+Nevirapine (NVP) or Zidovudine+Lamivudine+Efavirenz regimen. Venous blood samples were collected to measure trans aminotransferases (ALT and AST) and alkaline phosphatase (ALP), using colometric enzymatic reaction which were used to classified hepatotoxicity based on age and sex.

**Results:** A total of 38 (38%) and 55 (55%) patients presented with hepatotoxicity while 15% and 28% of patients of them had severe hepatotoxicity at 4 and 24 weeks respectively. Serum levels of all enzymes increased significantly (p<0.05) with increased treatment duration. Univariate analysis revealed that the risk factor of developing severe hepatotoxicity was significantly (p<0.05) greater in patients <30 years, males, low BMI, low monthly income earners and patient on AZT+3TC+ NVP regimen. While multivariate analysis showed that age <30 years, Low BMI, low monthly income and the use of AZT+3TC+NVP was an independent risk factors.

**Conclusions:** Low BMI, <30years, low monthly income and the use of AZT+3TC+NVP regimen were identifiable risk factors for the development of severe hepatotoxicity. As such these factors should be considered as an important strategy by clinicians in preventing the hepatotoxicity.

#### **Recent Publications:**

- 1. Lem E A et al. (2018) Incidence of elevated aminotransferases levels among patients presenting with hepatitis syndrome in the northwest region of Cameroon. Cohesive J. Microbiol. Infect. Dis. 1(1):1-5.
- 2. Lem E A et al. (2017) Knowledge, practice and prevalence of *Helicobacter pylori* infection in the north west region of Cameroon. Clinical Biotechnology and Microbiology. 1(4):135-143.
- 3. Lem E A et al. (2017) Hepatotoxicity and anaemia co-morbidity in treated HIV patients in Fundong subdivision in the northwest region of Cameroon. Microbiology Research Journal International. 18(5):1-10.
- 4. Lem E A, Nyuydzedze S S and Ndifor G A (2016) Assessment of knowledge, attitude and practice towards hepatitis B among two rural communities of the anglophone regions in Cameroon. IRA-International Journal of Applied Sciences. 4(3):490-505.
- Lem E A and Penn K (2016) Assessing prevalence and risk factors of hepatitis B surface antigen amongst pregnant women attending antenatal clinic in the northwest region of Cameroon. European Journal of Research in Medical Sciences. 4(1):32-43.

#### Biography

Lem Edith Abongwa, a Medical Microbiologist is pursuing PhD from Kenyatta University, Kenya. She is also an Assistant Lecturer at the University of Bamenda, Cameroon. Her research interest is on HIV and Hepatitis B virus. She is interested in the identification and assessment of risk factors that expose communities to these infections and possible solutions to prevent and control them as well as parasite strain diversity and severity to infectious infection. Prior to medical research she was the Head of a public health non-governmental organization assessing the implementation of option B+ in two regions of Cameroon sponsored by a PEPFAR HIV/AIDS project in Cameroon.

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### Noninvasive prediction of portal hypertension and liver fibrosis

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**P**ortal hypertension (PH) is responsible for most of the complications that mark the transition from compensated to decompensated cirrhosis, namely variceal hemorrhage, ascites and hepatic encephalopathy. Due to the invasiveness, requirement for advanced technical expertise and high costs associated with HVPG measurements, the introduction of simple, noninvasive screening and diagnostic methods would represent a great clinical advancement. The aim of this work is to evaluate the diagnostic efficacy of noninvasive liver fibrosis indexes in the diagnosis of PH. This is a prospective study conducted in the period 2012-2016 including 87 cirrhotic patients. These patients are admitted in the Department of Gastrohepatology at University Medical Center of Tirana Mother Teresa in Tirana and also followed at the policlinic specialities in Tirana. A multivariate logistic model of serum markers showed that AST-to-platelet (PLT) ratio index (APRI), AAR (AST/ALT ratio), Fib-4, fibrosis index (FI) were associated with PH. Also portal blood flow was measured and upper endoscopy was performed. Actually they couldn't undergo hepatic venous pressure gradient (HVPG) evaluation. For the diagnosis of cirrhosis AUCs were 0.879 and 0.851 for APRI and FIB-4 respectively and predicted the presence of clinically significant portal hypertension (CSPH), with the highest PPV (94%) and (93.3%). No significant difference was found between them and ROC curve for Echo Doppler (pairwise comparison of ROC APRI ~ Echo\_Doppler p=0.8 curves, Echo\_Doppler ~ Fib\_4 p=0.5). Noninvasive liver fibrosis indexes could be used not only as a first-line screening method for CSPH but also for predicting esophageal varices (EV) in cirrhotic patients as well as proxy for fluxmetric measurement.

#### **Biography**

Edlira Elezaj is a Gastrohepatologist in department of Gastrohepatology at University Hospital Mother Tereza, Tirana, Albania since the year 2005. Her occupational skills in General medicine was covered at University of Tirana. From 1998- 2005 her specialization course in Gastro Hepatology, Abdominal Exercise, Digestive Endoscopy were persued at the same university, University of Tirana. She is curently pursuing PhD on Noninvasive evaluation of portal hypertension. She is having 16 years of experience as Gastro-hepatologist from Regional Health Authority of Tirana, Polyclinic of Speciality No.2 and Tirana Continental Hospital. She was invited to many conferences and is Authoring 20 referral articles.

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### Liver mitochondria KATP channel is highly sensitive to KATP channel opener diazoxide

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The functional consequences of mitochondrial KATP channel (mKATP channel) opening in liver are less studied as compared with heart and brain. In this work we studied liver mKATP channel opening with KATP channels opener diazoxide without Mg·ATP. Using polarography and light scattering, we found that full activation by diazoxide occurred at <0.5  $\mu$ M with parallel increase in ATP-insensitive K<sup>+</sup>-uptake. The rise of diazoxide concentration up to 100  $\mu$ M augmented ATP-insensitive K<sup>+</sup>-uptake, but not mKATP channel activity. We concluded that native mKATP channel was by the order more sensitive to diazoxide without Mg·ATP, which shifted channel affinity to micromolar concentration level. Uncoupling effect of liver mKATP channel opening was estimated based on its share in oxygen consumption. Obtained results reveal novel aspects of mKATP channel properties. Based on the experiments, we hypothesized that native liver mKATP channel might comprise high affinity sites for diazoxide binding in the absence of Mg·ATP.

#### Biography

Olga V Akopova has specialized in Biochemistry and Physiology. She is a Principal Investigator in Circulation Department of A A Bogomoletz Institute of Physiology, National Academy of Science of Ukraine, Kiev, Ukraine. Her research interests include: 1) mitochondrial potassium transport. 2) mKATP channels, their cell-specific properties and the interaction with physiological and pharmacological ligands. 3) the impact of K<sup>+</sup> transport on mitochondrial bioenergetics and metabolism (reactive oxygen and nitrogen species production, Ca<sup>2+</sup> transport, ATP synthesis).

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### Metanalysis: Rebamipide a potential drug for GI protection against ASA gastroenteropathy

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**Background:** Aspirin has been used to lower the incidence of cardiovascular events but chronic used my lead to gastric mucosal damage that may lead to bleeding. Rebamipide is a gastro protective agent that may reduce the risk of GI bleeding on its pleiotropic effect by increasing gastric mucosal prostaglandin and gastric mucus production, scavenging of hydroxyl radicals, inhibition of neutrophil activation, suppression of gastric mucosal inflammation, regulation of apoptosis related genes and inhibition of tyrosine nitration.

**Objective:** To investigate whether a mucosal-protective agent, Rebamipide, could prevent gastric mucosal injuries induced by low dose Aspirin.

**Methods:** Bibliographical searches were performed using PubMed and Cochrane Library. Search terms included Rebamipide and Aspirin. A meta-analysis of all journals that were included in the inclusion criteria were reviewed comparing Rebamipide supplementation with non-Rebamipide containing therapy was performed.

**Results:** Three RCTs including 579 individuals were eligible. In general, Rebamipide acted better than placebo against Aspirininduced gastroduodenal injury. Rebamipide showed a beneficial effect against the mucosal GIT damage. Heterogeneity of population were computed using chi<sup>2</sup> which shows 2.31 (df of 2, P=0.31, I<sup>2</sup>=13%). Journals included in the study were Kazuhiro et al., with weight of 2.4%, OR of 0.13(0.02, 0.90); Takatsugu et al., with weight of 90.1%, OR of 0.32 (0.25, 0.41) and Toshio et al., with weight of 7.5%, OR of 0.16 (0.06, 0.47). Combining the three studies yields a total (95% CI) with OR of 0.31 (0.24, 0.39).

**Conclusion:** Current evidences show Rebamipide is effective and safe for defending against NSAID-induced gastroduodenal and lower-gastrointestinal injuries. However, more well-designed trials should be conducted to fully confirm the practical value of Rebamipide.

#### Biography

Bienvenido P Tiu Jr. is from Philippines. He graduated from University of Santo Tomas as Bachelor of Science in Biology. He continued his medical education at Far Eastern University - Nicanor Reyes Medical Foundation. He is currently a second year Internal Medicine resident in World Citi Medical Center.

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# Accepted Abstracts

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## Natural antiviral drugs as novel hepatitis b virus polymerase-inhibitors: Cell culture and molecular docking study

Mohammad K Parvez, Md. Tabish Rehman and Mohammed S Al Dosari King Saud University, KSA

repatitis B virus (HBV) causes chronic liver diseases, including fulminant liver failure, cirrhosis and hepatocellular Hepatitis B virus (HBV) causes chronic nyer diseases, including reacting about two billion of world population. Despite high anti-HBV efficacies, the nucleoside analogs (e.g., lamivudine) lead to the emergence of drug-resistance, interferons (e.g., IFN-a causes adverse side-effects. Comparatively, various natural or plant products have shown similar or even better efficacy. Hence, new antiviral strategies must focus not only on synthetic molecules but also on potential natural compounds. In this report, we have combined the in vitro cell culture and in silico molecular docking methods to assess the novel anti-HBV activity and delineate the inhibitory mechanism of selected plant-derived pure compounds of different classes. Of the tested (2.5-50 µg/ml) twelve non-cytotoxic compounds, ten (10 µg/ml) were found to maximally inhibit HBsAg production at day 5. Compared to quercetin (73%), baccatin III (71%), psoralen (67%), embelin (65%), menisdaurin (64%) and azadirachtin (62%) that showed high inhibition of HBeAg synthesis, lupeol (52%), rutin (47%),  $\beta$ -sitosterol (43%) and hesperidin (41%) had moderate efficacies against HBV replication. Further assessment of quercetin in combination with the highly active compounds, enhanced its anti-HBV activity up to 10%. Being the most important drug target, a 3D structure of HBV polymerase (Pol) was modeled and docked with the active compounds, including lamivudine as standard. Docking of lamivudine indicated strong interaction with the modeled HBV Pol active-site residues that formed stable complex ( $\Delta G$ =-5.2 kcal/mol). Similarly, all the docked antiviral compounds formed very stable complexes with HBV Pol ( $\Delta G$ =-6.1 to -9.3 kcal/mol). Taken together, our data suggest the anti-HBV potential of the tested natural compounds as novel viral Pol-inhibitors.

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## Incidentally detected space occupying lesions in liver imaging in chronic hepatitis C and the risk of hepatocellular carcinoma

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**Aim:** The aim of this study is to evaluate the occurrence and nature of space occupying lesions (SOL) on liver imaging in patients with chronic hepatitis C (CHC) receiving antiviral therapy (AVT).

**Methods:** 1540 patients (from January 2002 to July 2014) with CHC who underwent ultrasound (USG) scan, liver biopsy (LB) and received conventional (pegylated interferon and ribavirin) dual AVT were retrospectively analyzed for the occurrence and nature of SOL prior to initiation of AVT and thereafter.

**Results:** Mean age of patients were 41.9±9.7 years (85% males), predominantly genotype 4 (65%) and genotype 1 (11%). Pretreatment LB showed (Scheuer classification) stage-0 fibrosis (F0) in 1.9%, stage-1 (F1) in 32.9%, stage-2 (F2) in 39.5%, stage-3 (F3) in 19% and stage-4 (F4) in 6.6% patients. Median follow-up was 3.5 years (5390 patient years). Computed Tomography (CT) and Magnetic resonance imaging (MR) scans were performed in 1185 and 560 patients respectively prior to AVT and during follow up. Of the patients with F4 on LB, USG identified cirrhosis in 68%. Of all the patients reported with cirrhosis on USG, F4 was seen in 16.6% and advanced fibrosis (F3 and F4) in 53.4%. Routine pretreatment USG showed fatty liver in 334 (20.8%). Incidental SOL included, cysts in 21 (1.3%), hemangioma in 41 (2.6%) and hypoechoic lesions in 14 (0.9%). CT and/or MR scan did not change diagnosis in most of these SOL, except in two hypoechoic lesions detected pretreatment (one was confirmed as hepatocellular carcinoma (HCC) by CT and another by MR) and one hypoechoic lesion during post AVT follow up (confirmed as HCC in MR). CT and MR identified three and one HCC respectively that were missed on USG against cirrhotic background. Four patients had HCC during pretreatment evaluation and 11 developed new onset HCC during post AVT follow up. The mean alpha fetoprotein (AFP) at diagnosis of new onset HCC was 63.3±1173.8 (vs 16.2±118.1 for non HCC patients, p=0.001). Elevated AFP levels were seen in 81.8% of these patients. Independent pretreatment predictors of new onset HCC were pre-AVT albumin and GGT.

**Conclusions:** Most of the incidental SOL detected in routine pre-AVT USG retained diagnostic consistency with further radiological imaging with CT and MR. A predicting model including pre-AVT albumin and GGT showed high predictive accuracy for development of HCC during post treatment follow up; which could be used as a guide to consider further radiologic evaluation in these incidental SOL.

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## Bloodless liver resection for hepatocellular carcinoma (HCC) in cirrhotic patients using Habib sealer needle: An Egyptian single center experience study

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**Introduction:** The most common primary liver tumor is hepatocellular carcinoma. Hepatic resection remains the best treatment for liver tumors. In the absence of diffuse bilobar disease, vascular invasion or extrahepatic metastases, surgical management is indicated. Bleeding remains a significant factor affecting prognosis. The concept of introducing new bloodless techniques to facilitate surgical resection of liver tumors has stimulated hepatobiliary surgeons. This new procedure employs the heat produced by an RF needle electrode to coagulate the liver tissue before cutting it, thus permitting liver resection with reduced blood loss.

**Material & Methods:** Ninety sex liver cirrhosis patients with hepatocellular carcinoma (HCC) were included in this study. All patients were submitted to confirm the diagnosis of HCC and evaluate the patients' liver conditions (Child-Pugh classification). Outcome measures were operative time, intra-operative blood loss, complications, hospital stay and recurrence of HCC.

**Results:** In this study a total of 96 cases were presented- 60 men and 36 women, whose mean age was 57.5. 92 (95.8 %) patients were Child-Pugh class A and 4 (4.2 %) were early class B, before treatment. Mean MELD (Model for End-Stage Liver Disease) score was 5. Mean platelets number was 154,250. Mean INR level was 1.18 (ranges from 1 to 1.4). Most of the patients 85 (88.5%) in this series had a solitary tumor, 10 patients (10.4%) had tow lesions excised and one patient had three lesions excised. The mean operative time was 113.4 minutes. The mean operative blood loss was 300 CC (range from 50 to 1200 cc) and the mean blood loss during parenchymal transection was 150 cc. The mean amount of blood transfusion 0.31 blood units (ranged from 0 to 2). The mean hemoglobin concentrations before and after the operation were 13.1, and 12.23 mg/dl respectively. The mean hospital stay time was 4 days.

**Conclusions:** This technique reduces the anesthetic time, operative time, and amount of blood loss. These are significant improvements for both the patient and the surgeon. Liver resection becomes a less risky surgical procedure; it eliminates the need for intensive care unit facilities; and less postoperative mortality and morbidity is encountered because of the smaller surgical insult to the patient.

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## *In vivo* cellular and molecular gastroprotective mechanisms of chrysin: Emphasis on oxidative stress, inflammation and angiogenesis

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astric ulceration is one of the major gastrointestinal disorders affecting people worldwide. Despite medical advances, J management of gastric ulcer and its complications remains a challenge facing medicine nowadays. In addition, currently available medicines exhibit limited efficacy and several side effects. Hence, the potential protective effects of chrysin -naturally occurring flavonoid- were tested against indomethacin-induced gastric ulcer model in rats. In a preliminary study, chrysin was administered to sprague-Dawly rats (200-220 g) at three different doses; 25, 50 and 100 mg/kg, single oral dose (S.O.D) compared to omeprazole given at a dose of 30 mg/kg, S.O.D. Indomethacin was administered at a dose of 48 mg/kg, S.O.D. Chrysin in both doses; 50 and 100 mg/kg were effective in promoting mucus secretion and preventing the rise in ulcer and lesion indices, acid production and histologic changes induced by indomethacin. During investigation of the possible underlying mechanisms, chrysin pretreatment significantly attenuated indomethacin-induced oxidative injury proved by its effects on catalase, reduced glutathione and lipid peroxidation levels. In addition, chrysin reduced inflammatory response caused by indomethacin owing to its effects on nuclear factor-kappa B (NF- $\kappa$ B), tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) and interleukin-1 $\beta$ (IL-1β). Moreover, chrysin activated peroxisome proliferator activated receptor- (PPAR-) leading to a phenotypic switch from pro-inflammatory M1 macrophages to the anti-inflammatory M2 macrophages evidenced by the upregulated mRNA expression levels of PPAR- and M2 marker genes (Arg-1 and CD206) and downregulation of M1 marker genes (IL-6 and CCL3). Furthermore, chrysin initiated angiogenesis via increasing expression of vascular endothelial growth factor (VEGF), basic fibroblast growth factor (bFGF) and cluster of differentiation-31 (CD31) resulting in tissue repair. Collectively, these findings indicate that chrysin possesses a potential protective effect against indomethacin-induced gastric ulcer via suppressing oxidative stress, inflammation and initiating angiogenesis.

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### Laparoscopic versus open approach in management of hepatic hydatid cystic disease

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**Introduction:** Hydatid disease has a worldwide distribution and commonly seen in sheep rearing areas. Tapeworm of genus Echinococcus is the parasite causing the disease. The most common site of involvement is the liver. Treatment options are medical therapy, percutaneous drainage, or surgical intervention.

**Objectives:** Assessment of the outcome of either laparoscopic or open surgical treatment of liver hydatid cyst.

**Patients & Methods:** Forty eight patients with liver hydatid cysts underwent either laparoscopic or open surgical approach under cover of albendazol therapy. Both were divided in two groups according to the procedure done. The data collected were demographic data, laboratory results, radiological tests, type of surgical intervention, and post-operative data.

**Results:** The study involved 25 male and 23 females with a mean age of 36.76. Twenty patients (41.66%) had laparoscopic approach and 28 patients (58.34%) had open approach. Forty six patients had 1 cyst and two patients had 2 cysts (P-value=0.787). According to type of operative procedure: deroofing was done in 38 patients, while resection was done in 8 patients. Only 2 patients had pericystectomy. With respect to packing of the cyst with omentum, it was applied in 23 patients of open approach group and 9 patients of laparoscopic approach group (P-value=0.013). The mean time of operation in the laparoscopic group was  $74.75\pm18.67$  minutes while in the open group was  $92.24\pm20.94$  minutes (P-value=0.004).

**Conclusions:** Hydatid cystic lesions of the liver can be treated either by laparoscopic or open surgical techniques with similar outcomes but with superiority of the laparoscopy due to less operative time and hospital stay.

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#### Fecal microbiota transplantation is a rescue treatment modality for refractory ulcerative colitis

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**Background & Aim:** Fecal microbial transplantation (FMT) provides to replace beneficial bacteria with more favorable microbiomes in recipient with dysbiosis. The aim of the present study is to prospectively investigate the efficacy of FMT by assessing the clinical and endoscopic response in patients with ulcerative colitis (UC) who had failed anti-inflammatory, immunosuppressive and TNF- $\alpha$  inhibitors (Infliximab, Adalimumab) and therapy.

**Methods:** In this prospective and uncontrolled study, 79 patients with UC were included. All medications except mesalazine were stopped 1 week before FMT. Colonoscopy was performed both before and after FMT. To assess the efficacy of FMT, Mayo scores were calculated at week 0 and week 24. A total of 500 ml extracted fresh fecal suspension was administered into the 30 to 40 cm proximal of terminal ileum of recipients.

**Results:** After 3 years of FMT experience with 79 patients who have completed their 6 months on UC and different 184 FMT, 31 of the (39.2%) 79 patients showed clinical response (100% clinical + labaratory + fully responded endoscopically), and 23 of the 79 (29.1%) patients achieved clinical and endoscopic remission (labarotory 70%, clinically and endoscopically 50-75% improvement) at week 24. Twenty patients (25.3%) were accepted as a nonresponder at the end of the week 24. There was no significant difference among donors concerning both the rate of clinical remission and clinical response. No adverse events were observed in the majority of patients during FMT and 24 weeks follow-up. Twenty five patients (31.65%) experienced mild adverse events such as nausea, vomiting, abdominal pain, diarrhea, and fewer after FMT.

**Conclusions:** FMT could be considered as a promising rescue treatment modality before surgery in patients with refractory UC. Besides, although the long-term results are unknown, FMT also appears to be definitely safer and more tolerable than the immunosuppressive and TNF- $\alpha$  inhibitors (Infliximab, Adalimumab) therapy in patients with UC.

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### Prevelance of occult HBV in chronic hepatitis C and cryptogenic hepatitis patients

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ccult hepatitis B Virus (HBV) infection (OBI) is considered as the possible a phase of the HBV natural history but it remains unclear the molecular mechanisms and clinical impact and epidemiology aspect of OBİ. We investigated the prevalence of OBI and its clinical impact among patients with Hepatitis C virus (HCV) infection and with cryptogenic hepatitis. This study protocol was approved by the ethics committee of İstanbul University- School of Medicine (No: 2015/1519). This prospective cohort study included a total of 60 HBsAg-negative patients (27 patients with chronic HCV and 33 patients with cryptogenic hepatitis) were enrolled in Department of Gastroenterology, Istanbul Faculty of Medicine. Liver tissue samples had been obtained by percutaneous needle liver biopsy and immediately frozen and stored at -80°C. Total nucleic acids were extracted from frozen liver biopsies using QIAamp DNA Mini Kit (Qiagen) according to the manufacturer's instructions. OBI was defined as HBV DNA positivity in two or more different viral genomic regions by nested polymerase chain reaction PCR using 4 sets of primers in preS-S (S), precore-core (C), Pol, and X viral regions of the HBV genome. Plasmid HBV DNA 4.1 kb and liver biopsy samples obtained from patients with chronic HBV infection (positive control) were used. Statistical analyses were evaluated using Mann-Whitney U, Chi-square test and Kruskal Wallis tests. The baseline characteristics of patients are presented in figure 1. The prevalence of OBI was 25.9% (7/26) with 27.3% (9/33), 26.7% (16/60) in patients anti-HCV (+), cryptogenic hepatitis, and totaly respectively. There wasn't significant differences for prevelance of OBİ between patients with Chronic HCV infection and cryptogenic hepatitis (P=0.907). Patients with anti-HCV (+), OBİ (+) were older compared with patients anti-HCV (+), OBİ (-), (P: 0.033). As it is expected that cryptogenic hepatitis patients had higher serum alkaline phosphatase and gamma-glutamyltransferase level. Clinical signifance and role of OBI in patients with chronic HCV infection is controversial. According to first results of the study, prevelance of OBİ is correlated with endemicity of Hepatitis B infection moreover OBİ can be associated with liver injury rather than chronic HCV infection. Therefore, it appears that host factors rather than viral factors are more responsible for OBI.

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### Febuxostat versus placebo or allopurinol for gout or asymptomatic hyperuricemia: A systematic review and meta-analysis

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**Background/Introduction:** Gout is one of the most common rheumatic diseases in humans characterized by increased serum uric acid level) above of 7 mg/dl in men and 5.7 in women while deposition of uric acid crystals in the joints. Urate lowering therapy (ULT) is the novel treatment for patients with gout. There is an ongoing debate about using which of the urate lowering therapies should be preferred

**Aim:** The aim of this study is to systemically review the literature and statistically analyze the safety and efficacy outcomes of febuxostat versus allopurinol in the treatment of gout or asymptomatic hyperuricemia.

**Methodology:** We searched 12 electronic medical databases and included randomized clinical trials (RCTs) comparing clinical outcomes between febuxostat and allopurinol in patients with gout or asymptomatic hyperuricemia.

**Results:** Nine RCTs were included in our meta-analysis. Febuxostat had significantly higher incidence of serum urate at last 3 monthly visits (RR=2.26, 95% CI [1.82, 2.80], p<0.00001) and at last visit (RR=1.81, 95% CI [1.65, 1.98], p<0.00001) compared to allopurinol. Mean change from baseline of serum urate <6.0 mg/dl at last 3 monthly visits was significantly lower in febuxostat than allopurinol (SDM=-0.84, 95% CI [-1.14, -0.55], p<0.00001). While, regarding serum urate <360 mg/dl at last 3 monthly visits, mean change from baseline did not favor any of the compared groups. No significant difference was detected between febuxostat and allopurinol in terms of safety outcomes such as, any adverse events, treatment related adverse event, events leading to discontinuation, serious adverse events, liver or renal function test abnormalities, abnormal electrocardiograph, abnormal urine protein or glucose, headache, upper respiratory infection, or gastrointestinal disorders.

**Conclusions:** Based on our study, febuxostat showed higher incidence of serum urate at last three-monthly visits and last visit than allopurinol. While, febuxostat and allopurinol were comparable in terms of safety outcomes.

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