**Tropical Medicine**

**Computer based algorithms and predictive models for the outcome of concomitant hepatitis C and thalassemia**

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As Iron overload and hepatitis C virus (HCV) infection together can lead to chronic liver damage in thalassemia major (TM) patients. Treatment endpoint is SVR defines as undetectable HCV RNA 24 weeks following termination of therapy. These considerations led us to design a prediction model in combination of data mining techniques to compare treatment efficacy and tolerability pegylated interferon (PeG-IFN) and ribavirin (RBV) combination therapy versus Peg-IFN monotherapy and estimated SVR were 65.1%, 70.9%, respectively. We investigated the role of iron overload on the efficacy of anti-HCV treatments. Various cutoff levels of ferritin were related to different probability of SVR. Finally, we evaluated the changes in blood transfusion regime, ferritin levels, laboratory and histopathological data during the antiviral treatment. Data from patients with β-thalassemia infected with hepatitis C virus genotype 4 from different centers in Egypt were analyzed. The main Objective of this paper is to classify data and assist the users in extracting useful information from data and easily identify a suitable algorithm for accurate predictive model from it. From the findings it can be concluded that J48 and CART are the best performance algorithms as a rule based classifier in comparable with different classification algorithms because they achieved maximum accuracy, maximum ROC, had least mean absolute error and it took minimum time for building this model through Explorer and Knowledge flow Results. This was further confirmed by univariate logistic regression analysis; p value < 0.01.

**Conclusion:** Baseline Ferritin Levels were significantly related to SVR in an HCV population as demonstrated by data mining.

**Liver fibrosis progression, treatment and health-related quality of life in thalassemia patients with chronic hepatitis C: a large, prospective, longitudinal study**

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**Background/Aims:** Patients with transfusion-dependent thalassemia and hepatitis C (HCV) are at risk of developing variable degrees of liver fibrosis. Liver biopsy, the standard of reference for assessing liver fibrosis, is an invasive and expensive procedure. Thus, we assessed the patterns of liver fibrosis progression rate in thalassemic patients with and without chronic HCV and compared the performance of transient elastography (TE) and a panel of non-invasive fibrogenic markers alone or in combination to liver biopsy for detecting the stage and progression rates of hepatic fibrosis.

**Methods:** In this prospective, longitudinal, study, we assessed the fibrosis progression rates in well-characterized cohorts of thalassemia patients with and without chronic HCV and patients with chronic HCV. The true fibrosis progression rate was calculated from paired liver biopsies. TE, YKL-40, transforming growth factor β1 (TGF-β1), hyaluronic acid, N-terminal procollagen III propeptide (PIINP) and cytokeratin 18 (CK 18) were measured at baseline and annually. Results were
compared and correlated to histopathologic findings and fibrosis progression rates.

Results: The fibrosis progression rates were significantly higher in patients with chronic HCV and thalassemia (0.48 ± 0.29) compared to those with chronic HCV (0.13 ± 0.25) or thalassemia (0.28 ± 0.31) (P < .0001). A direct linear correlation was observed between the progression of fibrosis rate/year and the progression rates of TE (r = 0.899, P < .001), YKL-40 (r = 0.730, P < .001), TGF-β1 (r = 0.626, P < .001), CK-18 (0.573, P < 0.002) and PIIINP (0.471, P = 0.03). SF-36 showed statistically significant differences in physical component scale (PCS) between thalassemia patients with and without chronic HCV infection.

Conclusion: Liver fibrosis is significantly accelerated in patients with chronic HCV and thalassemia. Transient elastography and serum direct fibrosis can be used, alone or in combination, as reliable non-invasive markers for detecting the stage of hepatic fibrosis and evaluating disease progression and monitoring of thalassemic patients with and without chronic hepatitis C.

Modern cutting-edge technologies: endoscopic submucosal dissection (ESD) and peroral endoscopic myotomy (POEM)

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Advanced endoscopy recently includes new cutting-edge technologies such as endoscopic submucosal resection (ESD). ESD is now a well-established endoscopic procedure for treatment of premalignant and early-stage malignant lesions such as of the stomach, esophagus, and colorectum (large colorectal polyps removal and for treating early-stage colorectal neoplasms with a maximum tumor size of 2–5 cm) providing a complete, endoscopic excision difficult to resect by conventional EMR with low local recurrences. For Barret’s carcinoma E(M)R suck and cut with cap (16 mm) remains the gold standard compared with ESD with water-jet. Always, proper patient and lesion selection for ESD are essential. Improved techniques and devices have been developed to facilitate safer and more reliable ESDs. Other modern cutting edge technique is peroral endoscopic myotomy (POEM), a revolutionary treatment for achalasia. It involves creating a submucosal tunnel directly to the stomach side; creating a submucosal tunnel into the gastric cardia and the adequacy of myotomy, important determining factors to success of POEM. High rates of esophagitis after POEM procedure shown by Western POEM experience Results. Controlled trials are still awaiting and POEM may not be superior to Heller myotomy and pene-modillation.

A systemic evolutionary approach to cancer: hepatocarcinogenesis as a paradigm

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The systemic evolutionary theory of cancer pathogenesis postulates that cancer is generated by the de-emergence of the eukaryotic cell system and by the re-emergence of its archaea (genetic material and cytoplasm) and prokaryotic (mitochondria) subsystems with an uncoordinated behavior. This decreased coordination can be caused by a change in the organization of the eukaryote environment (mainly chronic inflammation), damage to mitochondrial DNA and/or to its membrane composition by many agents (e.g., viruses, chemicals, hydrogenated fatty acids in foods) or damage to nuclear DNA that controls mitochondrial energy production or metabolic pathways, including glycolysis. Here, we postulate that the two subsystems (the evolutionarily inherited archaea and the prokaryote) in a eukaryotic differentiated cell are well integrated, and produce the amount of clean energy that is constantly required to maintain the differentiated status. Conversely, when protracted injuries impair cell or tissue organization, the amount of energy necessary to maintain cell differentiation can be restricted, and this may cause gradual de-differentiation of the eukaryotic cell over time. In cirrhotic liver, for example, this process can be favored by reduced oxygen availability to the organ due to an altered vasculature and the fibrotic barrier caused by the disease. Thus, hepatocarcinogenesis is an ideal example to support our hypothesis. When cancer arises, the pre-eukaryote subsystems become predominant, as shown by the metabolic alterations of cancer cells (anaerobic glycolysis and glutamine utilization), and by their capacity for proliferation and invasion, resembling the primitive symbiotic components of the eukaryotic cell.

The diagnostic and prognostic performance of transforming growth factor-β1 and survivin as non-invasive biomarkers for hepatitis C related hepatocellular carcinoma: a longitudinal study

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Background: To date, there are no reliable biomarkers for hepatocellular carcinoma (HCC). Tumor growth factor-β1 (TGF-β1) and survivin play a role in cancer cell proliferation, however, they are not adequately assessed in HCC. The current study evaluated TGF-β1 and Survivin as potential diagnostic and prognostic biomarkers for screening, early diagnosis and predicting outcome of hepatitis C (HCV) associated HCC.

Patient and Methods: Serial serum TGF-β1 and survivin were measured by ELISA in patients with proven HCC, cirrhosis and chronic HCV and correlated with intrahepatic TGF-β1 gene expression (RT-PCR), survivin (immunohistochemistry) and the percentage of apoptotic cells (apoptotic index; AI; TUNEL assay) as well as with clinical, pathologic data, prognosis and survival.

Results: A total of 75 patients (42 patients with HCC, 21 with cirrhosis and 24 with chronic hepatitis C virus (HCV) were enrolled ad prospectively followed. TGF-β1 levels were significantly higher in HCC patients (626.93 ± 34.90 pg/ml) compared to patients with cirrhosis (158.35 ± 22.1 pg/ml) and chronic HCV (63.67 ± 0.81 pg/ml) (p < 0.0001). Patients with HCC had baseline serum survivin levels > 90 pg/mL. Serum TGF-β1 and survivin levels significantly correlated with the intrahepatic TGF-β1 and Survivin expression (r = 0.873; p < 0.001 and 0.9014; p < 0.0001 respectively). Early HCC was associated with elevation of TGF-β1 and surviving. Serial serum TGF-β1 and Survivin levels