

UNIVERSITY OF MEDICINE AND PHARMACY OF CRAIOVA

***THE PREDICTIVE FACTORS OF SUSTAINED  
VIROLOGICAL RESPONSE AT PATIENTS  
INFECTED WITH HEPATITIS C VIRUS***

**-RESUME-**

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## **Key words**

Chronic hepatitis C virus; antiviral treatment; liver biopsy; immunohistochemistry; molecular genetics; real time elastography.

## **Introduction**

The hepatitis C virus represents one of the most common health problems of the world at this time and probably without a vaccin the epidemiological situation will aggravate. Romania is on the first place in Europa for the number of patients infected with hepatitis C virus, about 425000 to 600000.

## **Material and methods**

The study took place in the Medical One and Gastroenterology Cliniques of UMF Craiova and the Researche Center in Gastroenterology and Hepatology Craiova between january 2004 and december 2008.

From clinical, epidemiological, histological, immunohistochemical, genetical, imagistical studies we obtained the folows conclusions:

1. The lot we studied was composed by 150 patients with chronic hepatitis C witch

was treated with peginterferon and ribavirine.

2. Infection with hepatitis C virus was two times higher at women than men, between ages 55 to 60. The parenteral route of transmission was predominant.
3. The minor complications after liver biopsy (discomfort at the biopsy site or pain that needs analgesics and transient hypotension) was present at 30 percent of the patients. After liver biopsy none of the patients did not present major complications and nobody died after liver biopsy.
4. Through liver biopsy with Autovac automatic device and using Tru-cut needle of 1.4 mm it can be obtain optimal fragments for the histological analysis. The fragment obtained after liver biopsy is relevant for histological analysis only if it bring together the minimal number of complets portal space irrespective of his size.
5. The histological lesions was various being localised parenchymal and also mesenchymal level. The portal inflammation was suggested by inflammatory cells infiltrate composed by: lymphocytes, plasmocytes, fibroblasts.
6. The fibrosis was marked out by thin colagen fibers or fibrous scar localised in the portal or Diesse spaces. The fibrosis degree was higher after 50 years at women and it was correlated with hard-line histological activity.
7. Most of the patiens chronic infected with hepatitis C virus had various degrees of steatosis and advanced degree of fibrosis.
8. Immunohistochemical modern methods used to evaluating liver function brought more informations about pathological aspects in chronic hepatitis C.
9. The activation of stellate cells is the key events into liver injury and it is refering to the transition of the cell at rest rich of vitamin A into the cell full of fibrosis-the myofibroblast. Immunohistochemical, the myofibroblasts are detected through the alpha actins coloration. At patiens chronic infected with hepatitis C virus the marker intensity with alpha actins was correlated with the fibrosis degree. In this way, the alpha actin levels were small to moderate into mildly fibrosis, but it had high level in severe fibrosis where it was identified into the fibrosis scarrs and into cirrhosis noduls.
10. Into fetal liver, CK 19 was positive into the liver progenitor cells whereby it will

grow hepatocytes and also biliary cells. The liver progenitor cells reappear at adults into the liver regeneration process from chronic hepatitis and cirrhosis. At patients chronic infected with hepatitis C virus we identified progenitor cells using coloration with CK7 and CK19.

11. The marker for leukocyte common antigen is present into inflammatory infiltrate because it colors lymphocytes. The CD 45 immunomarker was negative into fetal liver but positive in chronic C hepatitis, being correlate with the histological activity degree.
12. There are a lot of methods to measure viral load but the tests effectuated in various labs can offer different results using the same sample. The viral load measurement using Cobas Amplicor method is the single approved by Food & Drug Administration. A lot of other techniques are in course of evaluation.
13. The ARN VHC detection using RT PCR is fast, tickle and cheaper towards Cobas Amplicor method. The sensitivity of RT PCR method recommend it for viral load monitoring of the patients chronic infected with hepatitis C virus with antiviral treatment. There is an inverse correlation between the abl-gene express and viral load detected through the two methods (Cobas Amplicor and RT-PCR).
14. The ultrasound elastography in real time is a new method for the evaluation of fibrosis. Through ultrasound elastography in real time it can be maken a difference between liver tissue with low density (fatty liver), liver tissue with moderate density (in chronic hepatitis) and hard line liver from cirrhosis.
15. The sustained virological response was obtained at less then a half from the lot of patients (43.24%) and youth normal weight, absence of steatosis and of cirrhosis were statistical correlated with the touch of sustained virological response.
16. A patient chronic infected with hepatitis C virus, young, with normal weight, mildly fibrosis and without steatosis has bigger odds to respond at the antiviral treatment towards an older patient, fatty, with severe steatosis and fibrosis.

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I followed several stages and courses in Romania and Europe, among which the most important are: EASL School of Hepatology: Hepatitis C & B, Milan 2005; Complications of liver cirrhosis and hepatocellular carcinoma Barcelona 2007; Postgraduate Course: The microscope at the bedside, Barcelona, 2007; Vascular Biology of the Liver in Health and Disease, Lisbon, 2008, EuroSchool Vascular Ultrasonography (2002), Interventional Ultrasound (2003), Breast Ultrasound (2004), Digestive Tumours (2005), Ultrasonography in Emergency (2006), Guidelines in gastroenterological Ultrasound (2007).

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**Published papers:**

- Larisa Săndulescu, Adrian Săftoiu, Daniela Dumitrescu, Tudorel Ciurea. Real-time Contrast-enhanced and Real-time Virtual Sonography in the Assessment of Benign Liver Lesions. *Journal of Gastrointestinal and Liver Disease*. 2008; 17: 475-479. ISSN 1842-1121
- Larisa Săndulescu, Adrian Săftoiu, Daniela Dumitrescu, Tudorel Ciurea. The Role of Real-time Contrast-enhanced and Real-time Virtual Sonography in the Assessment of Malignant Liver Lesions. *Journal of Gastrointestinal and Liver Disease*. 2009; 18: 103- 108. ISSN 1842-1121
- Rogoveanu I., Sandulescu Daniela Larisa, Gheonea D.I., Ciurea T., Comanescu V. Molecular bases of hepatic fibrogenesis – genetic and therapeutical implications in chronic viral C hepatitis. *Romanian Journal of Morphology and Embryology*. 2008; 49: 21-27. ISSN 1220-0522
- Filip M, Saftoiu A, Popescu C, Gheonea DI, Iordache S, Sandulescu L, Ciurea T. Postcholecystectomy syndrome - an algorithmic approach. *J Gastrointestin Liver Dis*. 2009; 18: 67-71.
- Larisa Sandulescu, A. Saftoiu, Simona Popa, T.Ciurea, Daniela Dumitrescu, C. Bataiosu, D.D.Ionescu. Particular echografic aspect of giant hepatic hydatid cyst asymptomatic. *Romanian Journal of Ultrasonography*, 2006;8; 4:235-241.
- Viorela Enachescu, Larisa Sandulescu, Simona Micu, Aurora Banta.

- Crioglobulinemy- extrahepatic manifestation in cronic viral C hepatitis. Craiova Medicala. 2008; 9; 1: 5-10.
- Larisa Sandulescu, Corina Voinea, Adrian Saftoiu, Dan Ionut Gheonea, Tudorel Ciurea, Ion Rogoveanu. The role of real-time ultrasound elastography as a non-invasive method for the assesment of liver fibrosis. Romanian Journal of Hepatology. 2008; 4: 26-35.
  - Larisa Sandulescu, Daniela Dumitrescu, Sevastita Iordache, Monalisa Filip, Dan Ionut Gheonea, Adrian Saftoiu, Tudorel Ciurea. Imaging approach in focal nodular hyperplasia a case report and review of the literature. Medical Ultrasonography. 2009; 2; 1: 37-42.
  - Rogoveanu, D.L. Sandulescu, T.Ciurea, D.I.Gheonea, V.Comanescu, P . Badea. The expression of liver progenitor cells-predictive factor of antiviral therapy response in patients with genotype 1 viral C chronic hepatitis. 42nd Annual Meeting of the European Association for the study of the liver, 11-15 aprilie 2007, Barcelona. Journal of Hepatology, Suppl.1, 46: S242-S243.
  - Iordache S, Saftoiu A, Ciurea T, Malos A, Gheonea DI, Filip M, Sandulescu L, Ioncica AM. The feasibility of contrast- enhanced endoscopic ultrasound in the assessment of tumour vascularisation in digestive cancer patients. The XX th Congress of European Federation of Societies for Ultrasound in Medicine and Biology, 31<sup>st</sup> May-3<sup>rd</sup> of June 2008, Timisoara. Ultraschall in der Medizin. Suppl 1, S30.
  - Sandulescu DL, Saftoiu A, Rogoveanu I, Ciurea T, Gheonea DI, Iordache S, Ioncica AM. The role of contrast-enhanced ultrasound in the characterisation of focal liver lesion. The XX th Congress of European Federation of Societies for Ultrasound in Medicine and Biology, 31<sup>st</sup> May-3<sup>rd</sup> of June 2008, Timisoara. Ultraschall in der Medizin. Suppl 1, S30.
  - I. Rogoveanu, D.L. Sandulescu, M. Ioana, D.I. Gheonea, T. Ciurea. Screening of genes associated with HCV- induced interferon resistance in hepatitis C virus genotype 1 infection. 43rd Annual Meeting of the European Association for the study of the liver, 23-27 aprilie 2008, Barcelona Journal of Hepatology, 48 (Suppl 2): S205

- A Săftoiu, DI Gheonea, T Ciurea, F Gorunescu, M. Gorunescu, S Iordache, L Sandulescu. Clustering algorithms in assessing the inter and intraobserver variability of real-time elastography for non-invasive assessment of diffuse hepatopathies. 16<sup>th</sup> United European Gastroenterology Week, Viena, Austria 18-22 October 2008, Gut/Endoscopy 57 (Suppl. II), A163: P0288.