VIRAL HEPATITIS AND THE ESTIMATIONS OF THE EFFECTS OF ANTIVIRAL TREATMENT

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ABSTRACT. For a long time, fibrosis was assessed only through hepatic biopsy puncture (PBH). The disadvantage of invasiveness and limitations of this method are the source of research for identification of alternative tests, noninvasive for fibrosis assessment, already grouped in serological scores or imaging methods (transient elastography). Diagnosis, eligibility, selection and monitoring regimen during antiviral therapy of patients with chronic hepatitis and HCV hepatic cirrhosis were established according to the therapeutic protocol in chronic hepatitis and compensated cirrhosis with HCV virus. This protocole is included in order MS / CNAS no. 1.301/500 from 11 July 2008 (* updated *) for approval of therapeutic protocols regarding medicine prescription, correspondent to international common names common names provided in the list including the relevant international medicines that insured persons, with or without personal contribution benefit of, on prescription, in health insurance system, approved by Government Decision no. 720/2008. Of the total patients who had received antiviral treatment two thirds were female. Numerical ratio between men and women varies by age, being almost equal before 40 years and over with increasing age. Initial viremia does not correlate with the amount of cytolysis or histological damage, but a higher value may influence response to treatment. Vast submitted is correlated with a higher viral load and a higher score of inflammation and fibrosis. Early viral response, accepted as a predictor for sustained response was present in 91 % of patients treated. The study showed a significant reduction of hepatic cytolysis after treatment and if at first the majority of patients have values 2-3 times upper limit of normal, after 6 months 77, 27 % had normal transaminases. Lack of a significant percentage of patients who do not respond early was an impediment in determining predictive factors for lack of response to therapy. However we found a better response in those with lower viremia and females.

Keywords: viral C hepatitis; antiviral treatment; hepatic fibrosis

INTRODUCTION

Chronic hepatitis C (HCV) is a public health problem, both at national and global level. Complex pathologic connotations highlighted so far make out of C chronic viral infection a disease that should not be limited to the liver, but seen as a metabolic disease that involves high prevalence of steatosis.

Hepatic steatosis in turn favors the progression of liver fibrosis and influences the rate of sustained virologic response (SVR). Detailed investigation of factors that contribute to suboptimal rate of SVR and their potential change in treatment are still topics of study.

On the other hand, the natural history of HCV involves the progressive aspect of liver fibrosis with possible development to cirrhosis, with all its complications. In this context, the assessment of fibrosis in chronic hepatopathies (chronic liver disease) is useful not only in stadialization of the disease and prognosis prediction, but also in establishing the optimal timing for treatment strategies.

For a long time, fibrosis was assessed only through hepatic biopsy puncture (PBH). The disadvantage of invasiveness and limitations of this method are the source of research for identification of alternative tests, noninvasive for fibrosis assessment, already grouped in serological scores or imaging methods (transient elastography).

Most tests have been validated and recommended as initial assessment of fibrosis in hepatitis C virus infected patients without other comorbidities, patients that have not been treated previously. There are few studies on the prospective assessment in dynamics of liver fibrosis through noninvasive methods in treated patients or in natural evolution. If at present time, various noninvasive methods have shown advantages in the assessment of liver fibrosis at the start of treatment, we consider that their usefulness can be tested in prospective follow up of these patients.

The optional theme of this thesis relates to the following:

- Widespread hepatitis C virus in relation to the numerous ways of transmission;
- The importance of pathogenic potential of chronic infection with HCV (more than 85 % of acquired infections and chronic infection can progress to cirrhosis and cancer on the liver);
- Insufficient data regarding incidence and clinical evolution of the disease in territorial profile;
- The need to estimate the therapeutic effects of the main resources of available antiviral treatment.

In relation to the grounds, the personal side of the paper refers to the following objectives:

A. Estimating the number of patients who undergo antiviral treatment;

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B. Research of correlation between patient age, viral load, liver cytolysis and histological damage.

MATERIALS AND METHODS

Lot selection taken into study

Diagnosis, eligibility, selection and monitoring regimen during antiviral therapy of patients with chronic hepatitis and HCV hepatic cirrhosis were established according to the therapeutic protocole in chronic hepatitis and compensated cirrhosis with HCV virus. This protocole is included in order MS / CNAS no. 1.301/500 from 11 July 2008 (* updated *) for approval of therapeutic protocols regarding medicine prescription, correspondant to international common names common names provided in the list including the relevant international medicines that insured persons, with or without personal contribution benefit of, on prescription, in health insurance system, approved by Government Decision no. 720/2008. Thus:

• **Acute hepatitis with HCV**
Criteria for inclusion in treatment:
- Biochemical: ALT> N;
- Virology: - AcHCVc-IgM positive, HCV RNA positive.
Treatment schedule:
- Pegylated interferon alfa-2a   180 mcg / week + ribavirin:
- 1,000 mg / day for body weight <75 kg;
- 1200 mg / day of body weight> 75 kg
   for a period of 24 weeks;
- Pegylated Interferon alfa-2b 1.5 mcg / kg / week + ribavirin:
- 1,000 mg / day for body weight <75 kg;
- 1200 mg / day of body weight> 75 kg
   for a period of 24 weeks for monitoring HCV RNA 4, 12, 24, and 48 weeks
• **Chronic hepatitis with HCV**
1. Chronic hepatitis with HCV - naive patients
  1.1. Chronic hepatitis with HCV
- Criteria for inclusion in treatment:
- Biochemical: normal or elevated ALT;
- Virology: HCV RNA detectable;
- Histologically: - liver biopsy, FibroMax with: A> / = 1, F> / = 1 and / or S> / = 1 or Fibroscan F> 1
Age: - </ = 65 years;
-> 65 years - the risk of comorbidities based therapeutic will be assessed*)
 *) Are excluded from interferon therapy patients with:
- Neurologic diseases;
  - mental illness (dementia etc.).
  - uncompensated diabetes;
  - autoimmune diseases;
  - ischemic heart disease or severe uncontrolled heart failure
  - severe respiratory disease, uncontrolled:
- Hb <11 g / dL;

- number of WBCs (the number of leukocytes) <5.000/mmc;
  - number of PMN <1.500/mmc.
  Treatment schedule:
- Pegylated Interferon alfa2a 180 micrograms / week + ribavirin:
  - 1,000 mg / day for body weight <75 kg;
  - 1200 mg / day of body weight> 75 kg;
  or
- Pegylated Interferon alfa2b 1.5 micrograms / kg / week + ribavirin:
  - 1,000 mg / day for body weight <75 kg;
  - 1200 mg / day of body weight> 75 kg.

Evaluation of treatment response

Definitions of treatment response:
 - RVR (Rapid Virologic Response / rapid viral response) = negativity of HCV RNA after 4 weeks of therapy;
 - EVR (Early Virologic Response / early viral response) = negativity or decrease> / = 2 log10 HCV RNA after 12 weeks of therapy;
 - Non Response (no response) = decrease in HCV RNA by <2 log 10 to 12 weeks of treatment;
 - Slow Response (Slow response) = HCV RNA negativity at 24 weeks;

 - EOT (End of Treatment Response / Reply viral end of treatment) = undetectable HCV RNA at end of treatment ;
 - SVR (Sustained Virologic Response / SVR) = undetectable HCV RNA 24 weeks after completion of therapy ;
 - Breaktrough = detectable HCV RNA during treatment , after EVR ;
 - Relapse (Relapse) = a positive HCV RNA after achieving viral response at the end of treatment .
  The initial response to therapy is assessed:
- Biochemical: normal ALT ;
- Virological : HCV RNA decline > / = 2 logs below the limit of 4 , 12 or
  24 weeks .
  HCV RNA was determined :
   - at the beginning of therapy ;
   - after 4 weeks of therapy ;
   - at 12 weeks of therapy if detectable HCV RNA at week 4 ;
   - at 24 weeks of therapy if not achieved negativity, but decrease was obtained
  > / = 2 log10 HCV RNA after 12 weeks of therapy ;
   - at the end of therapy (48 weeks of therapy at the time of HCV-RNA negativity) ;
   - at 24 weeks after the end of therapy.
  Duration of treatment:
   - 24 weeks for genotype 2 - 3 (+ ribavirin 800 mg / day);
   - 24 , 48 or 72 weeks for genotype 1-4 as follows :

- if the initial HCV-RNA is < 600,000 IU / mL to give RVR (undetectable HCV RNA at week 4), 24 weeks of treatment are carried out;

- if at 12 weeks from therapy start HCV-RNA is detectable, the treatment is continued for up to 48 weeks.

- if at 12 weeks after start of therapy of HCV-RNA detectable but reduced by> / = 2 log compared to before treatment, continued treatment for up to 24 weeks, when it makes a new determination of HCV-RNA; - if HCV-RNA is positive at 24 weeks, the treatment is stopped;

- if HCV-RNA is negative at week 24, treatment is continued for up to 72 weeks.

To achieve the objectives we have studied treatment records of 122 patients accepted for making antiviral therapy with Peg- interferon and ribavirin from 1.01.2009 to 31.12.2010 continuing to follow patients until treatment completion.

On these patients liver biopsy was performed, and from 100 of them biological samples were collected in order to determine serum biomarkers.

Given that in histopathological diagnosis of liver fibrosis, correlation with clinical data is important, we have studied the clinical observation sheets (hospitalized patients), patient records (for the ambulatory consult) and also data from the anatomopathologic record of these cases. Current medical records (for patients admitted during the concomitant study period) and archive (retrospective study) have been studied, from which we have selected a number of clinical data such as: patient age, reasons for hospitalization, personal history, subjective clinical signs that have determined patients to present to the doctor, objective clinical signs targets - local clinical examination, laboratory tests (previous biopsies, computed tomography, ultrasound) and presumptive clinical diagnosis.

We have studied the parameters included in the national tracking treatment of chronic hepatitis C, comparing data from different points of evaluation.

Paraclinical investigations

Assessment of liver fibrosis was performed using the following laboratory investigations:
- Liver biopsy;
- FibroMax investigation.

Liver puncture biopsy

Biopsy is performed in the intercostal space/area corresponding to the point of maximum liver dullness between the anterior and posterior axillary lines. After fixing the place, the skin is sterilized with iodine and alcohol seeps into the skin intercostal space 2-3 ml of 1% lidocaine. It pierces the skin with stylet. The biopsy needle penetrates 4 cm, then is aspirated and punctured. Harvested fragment is inserted into the fixative. A macroscopic examination of the biopsy fragment is made and if not satisfactory repetition of biopsy is recommended.

Biopsy has some contraindications: patients who do not cooperate, prothrombin deficiency, local infection, ascites, jaundice intensive extrahepatic obstruction, marked anemia and prolonged bleeding from skin incision for biopuncture.

Reactions and complications are: pain at the site of penetration extending to the right shoulder, epigastric pain or discomfort, bleeding into the peritoneum. Although it is rare is the main lethal complication of liver biopsy outcome. Typically the bleeding is occurring during the 24 hours following the biopsy. Fortunately bleeding stops spontaneously and its consequences can be corrected by infusion of blood. Biliary peritonitis - can occur only if mechanical jaundice and may reflect accompanying bladder infection and the shock - very rarely occurs after biopsy. Fatal biliary embolism is a rare complication; was cited in a patient with carcinoma of the ampulla of Vater.

Liver biopsy shows some limitations in obtaining very small fragments insufficient for developing pathological diagnosis; occurrence of sometimes fatal complications of puncture biopsy; opposed to laparotomy where liver fragment can be chosen, biopsy can be performed in the best case under ultrasound.

The fragments are collected and processed to obtain histological sections.

To calculate the degree of histological liver damage, anatomopathological laboratory analyzing liver biopsy specimens collected uses modified Knodell score, which has the following components:

Table 9. Modified Knodell score

Apoptosis+ focal necrosis + inflammation	
1-4 foci/ field	Score 1-2
5-10 foci/ field	Score 3
Over 10 foci/ field	Score 4
Interface hepatitis (piecemeal necrosis)	
Absent	Score 0
In the focus	Score 1-2
Below 50% of the circumference	Score 3
Over 50% of the circumference	Score 4
The intensity of inflammation in the space port, diffuse or nodular distribution and composition	
Absent	Score 0
Slight	Score 1
Moderate or limited to the space port	Score 2
Moderate	Score 3
Marked	Score 4
Fibrosis	
Absent	Stage 0

In some portal areas with short septa	Stage I
In most areas of collagen deposition gates along sinusoids	Stage II
Fibrosis expansion of most portal areas with porto-portal bridges	Stage III
Expansion of fibrosis in portal spaces with porto-portal and porto-central fibrous septa	Stage IV
Porto-portal bridging fibrosis and porto-central boundary of nodules (incomplete cirrhosis)	Stage V
Regenerative nodules with fibrosis around	Stage VI

So, the maximum degree of necroinflammation may be 12 and from this point of view the severity of this damage is divided as follows:
- Mild chronic hepatitis: score 1-5;
- Moderate chronic hepatitis: score 6-8;
- Chronic severe hepatitis: score above 9.

FibroMax investigation developed by BioPredictive is a combination of five different non-invasive tests: FibroTest, ActiTest, SteatoTest, NashTest and AshTest. It is based on an algorithm that combines results from the determination of serum biochemical markers (alpha-2macroglobulin, haptoglobin, apolipoprotein A1, total bilirubin, gamaglutamil-transpeptidase - GGT, ALT alanine aminotransferase, aspartate-aminotransferase AST, fasting glucose, cholesterol, triglycerides) with age, sex, weight and height of the patient to assess liver damage. Thus:

- FibroTest measures the degree of fibrosis (F0-F4 corresponding stages of METAVIR score);

-ActiTest measures the degree of necro-inflammatory activity in patients with chronic viral hepatitis B or C (corresponding grades A0-A3 of the METAVIR score);

-SteatoTest assesses hepatic steatosis due to frequent increase in transaminases ALT and GGT (corresponding to stages 0-3 of steatosis: S0-S3);

-NashTest evaluates the presence of non-alcoholic steatohepatitis in obese patients with dyslipidemia, insulin resistance or diabetes (corresponding to the three degrees of classification of Kleiner: No "NOT NASH" N1 "borderline NASH" and N2 "NASH");

-AshTest measures the degree of liver damage in patients with excessive consumption of ethanol (corresponding to the 4 degrees H0-H3).

The technology developed by Biopredictive uses patented and scientifically validated algorithms, which are subjected to very strict quality control.

FibroTest (FT) was first used in patients with chronic hepatitis C; was subsequently validated in hepatitis B, hepatitis D, HIV coinfection, alcohol liver disease and non-alcoholic fatty liver. Thus FT is a universal marker of fibrosis, at least for the most common chronic liver disease. ActiTest is the only non-invasive marker validated in laboratory work necroinflamatorie used exclusively in patients with chronic hepatitis B or C. These two tests were added to the other three investigations that are designed to evaluate or aggravating factors associated fibrosis: steatosis liver (SteatoTest), non-alcoholic steatohepatitis (NashTest) or alcoholic steatohepatitis (AshTest). FibroMax allows a single procedure of these five tests.

Published studies have demonstrated predictive value and benefits of this investigation as an alternative to hepatic biopsy 2; 3; 4; 5; 6.

Patient Preparation – a jeun (required) [60].

Collected specimen - venous blood [60].

Container harvesting - vacutainer without anticoagulant with/without gel separator [60].

Required processing after harvesting - separate the serum by centrifugation; working in the same day; If this is not possible, the serum can be stored at 2-8 ° C or -20 ° C [60].

Causes of proof rejection- hemolyzed or lipemic specimens [60].

Volume of sample - minimum 3 ml of serum [60].

Stability test - separate serum is stable 3 days at 2-8 ° C and protected from light (for bilirubin); at -20 ° C for a long time [60].

Method – in Synevo laboratory dosing ten biochemical markers is performed by standardized methods in accordance with technical recommendations provided by BioPredictive:

• immunoturbidimetric method for alpha-2macroglobulin, haptoglobin and apolipoprotein A [60];

• enzymatic method with pyridoxal phosphate standardized according to IFCC for ALT and AST;

• enzymatic method standardized in relation to Szasz method for GGT;

• colorimetric method (diazo reaction) for total bilirubin.

• enzymatic method - colorimetric cholesterol, triglycerides and glucose.

Interpretation of results

The results obtained from serum markers are placed using a passcode in BioPredictive site where it will generate a report with scores of fibrosis, necroinflammatory activity, hepatic steatosis, non-alcoholic steatohepatitis, alcoholic steatohepatitis, for each patient tested [60].

FibroTest

The results are reported in degrees:

F0 - absence of fibrosis;

F1 - portal fibrosis;

F2 - fibrosis "bridged" with rare septa;

F3 - bridging fibrosis with numerous septa;

F4 - cirrhosis
ActiTest
Necroinflammatory activity is reported in degrees:
A0 - lack of activity;
A1 - minimal activity;
A2 - moderate activity;
A3 - severe activity;
SteatoTest
The results are expressed as a score:
S0 - the absence of steatosis;
S1 - minimum steatosis (<5% of hepatocytes with steatosis);
S2 - moderate steatosis (6-32% of hepatocytes with steatosis);
S3 - severe steatosis (33-100% of hepatocytes with steatosis);
NashTest
The result is framed in a group:
N0 - No NASH (non-alcoholic steatohepatitis without);
N1 - Borderline NASH (non-alcoholic steatohepatitis border);
N2 - NASH (non-alcoholic steatohepatitis present).
 AshTest
The result is framed in a group:
H0 - no alcoholic steatohepatitis;
H1 - the alcoholic steatohepatitis;
H2 – moderate alcoholic steatohepatitis;
H3 – severe alcoholic steatohepatitis 6.

Limits and interference

This test is not recommended in patients with acute hepatitis (increased ALT values), acute hemolysis (haptoglobin values decrease), acute inflammatory states (increasing values of alpha2-macroglobulin) or extrahepatic cholestasis.

In patients with chronic hemolysis or Gilbert's syndrome a visit to a specialist for interpretation will be required.

The test has not been validated in hepatic transplant patients 2; 6.

Statistical interpretation

To analyze quantitative data gathered during investigation, the first step was building the database and coding of variable values. Also, participants with incomplete data were eliminated from the study. Building the database was followed by two types of analysis: descriptive analysis and inferential analysis.

Descriptive processing

Descriptive analysis of the data was intended to illustrate the situation included in the study sample. Depending on the type of data two types of descriptive analysis were performed. In the cases of data presented as frequencies, frequence and percentage of effective sample or working groups was calculated.

Inferential processing

In order to test if the descriptive results obtained are statistically significant it was appealed to the calculation of inference tests by reference to the materiality threshold .05. Inferential processing was different depending on the nature of the data.

Thus, to calculate the significance of differences in frequencies it was calculated the value of hi square test. To test the significance of differences between means of two different groups (by gender or age) has been calculated the value of parametric t Student test for independent samples.

Correlation

The calculation of correlation indexes was used to test the association degree between two variables. A correlation coefficient can take a nil value from -1 to 1. If the correlation coefficient is closer to 1 or -1, the combination of the two variables is stronger. If a correlation coefficient has a positive value, then the association between variables is a proportional one – if one variable value increases so will the second one. A negative correlation indicates an inverse relationship between variables, which means that while the values of a variable increase, the values of the second variable decrease.

Correlation diagram, called the cloud of points, illustrates the relationship between two variables showing;

§ type of relationship – linear if the points tend to group by a line;

§ direction of the relationship - positive if the cloud of points is oriented from bottom to top and from left to right, negative if the cloud of points is oriented from top to bottom and from left to right;

§ the strength of relationship – the more stronger is the combination of variables is, the less scattered will be the point cloud.

Differences between averages

Testing differences between averages is different depending on the nature of the data, results distributions and scattering of obtained data. If the conditions of homogeneity (standard deviations have similar values), the results are evaluated on a scale interval (numerical) and results distributions are normal parametric statistical inference tests are used. These are more accurate than nonparametric tests, in their formula of calculation entering actual results achieved by the participants in the study.

If the three conditions mentioned above are not satisfied, nonparametric inference tests are used. They are less accurate than parametric tests, their calculation formula is based on actual ranks and frequencies, which are approximations of the actual values obtained from the participants. In this case it is probable we do not observe a significant difference between the two averages, even if it exists, so that type II errors are possible to appear.

To compare the significance of differences between means of two different groups we can use the

parametric test t Student for independent samples or Mann -Whitney U meparametric test.

Differences between the numbers of frequencies

To calculate the significance of differences in frequencies the value of hi square test has been calculated. There are two situations in which use different methods for calculating hi square test: hi square fit and hi square of independence.

Matching hi square is used to compare the numbers observed with theoretical numbers (ie numbers that would be obtained if the data would be due to chance).

Hi independence square (homogeneity) is for a situation where we want to study the relation between two variables or qualitative characteristics.

Prediction

To test the ability of prediction of some variables regression analysis is used. To this end it is tested to what extent certain variables, called predictors, can result in a particular outcome called criterion or dependent variable.

Regression analysis can be a simple one, when testing the predictive capability of a single predictor variable, or multiple, when several predictors are simultaneously taken into consideration.

Issues pursued for regression analysis are:

§ statistical significance of the regression model - if the model resulting from the regression analysis leads to a significantly better solution than the one based on the average;

§ percentage of explained variance - what percentage of results variance is explained by the predictors included in the regression equation; in this respect is referred to the value of R^2;

§ statistical significance of predictors - if predictors included in the regression equation contribute significantly to explain the results of the criteria; are significant predictors for which it is obtained a significance level less than .05;

§ sign of predictors, which in interprets only if they contribute significantly to the development of criteria; if the sign of the predictor is positive, we have a positive association between predictor and criterion, if the sign is negative, growth of predictor will decrease the criterion;

§ the weight of predictor, which is given by the value of regression coefficients and expresses the contribution of each predictor to the value of criterion.

When the criterion variable is dichotomous or categorical (has more than two discrete values), a logistic regression analysis is used. The working method is similar to that of single and multiple linear regression.

RESULTS AND DICUSSIONS

Estimating the number of patients who followed antiviral treatment

From 1.01.2009 to 31.12.2010 a number of 122 patients have followed antiviral treatment, whose diagnosis of viral infection with HCV was determined by the presence of anti-HCV antibodies in serum.
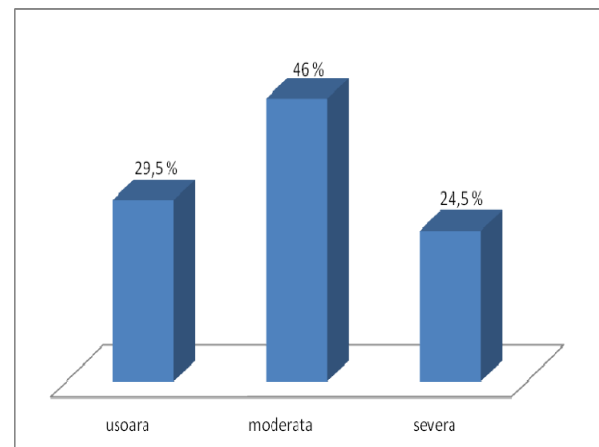
Fig.1. The degree of inflammation at the beginning of treatment

- stage of fibrosis: stage 0 - 18,30 %
- stage 1 - 30,07%
- stage 2 - 25,49%
- stage 3 - 15,03%
- stage 4 – 5,88 %
- stage 5 – 5,23 %
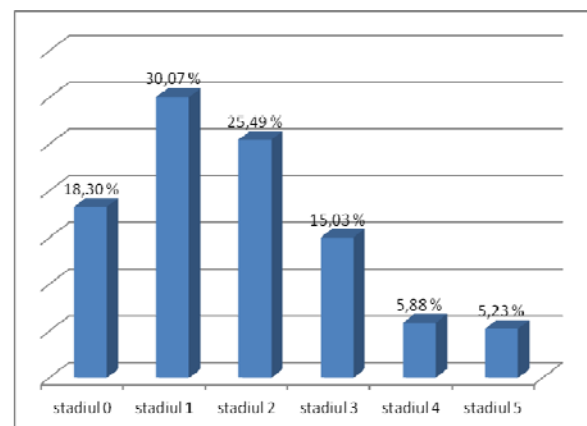
Fig. 2. Fibrosis stage when starting treatment

On anatomopathological examination the majority of patients (46%) had a moderate degree of liver inflammation. Regarding the stage of fibrosis, it has a more balanced distribution among candidates for treatment.

Study of viremia when starting treatment has shown very large variations of a few tens of thousands IU / ml to several million IU / ml.
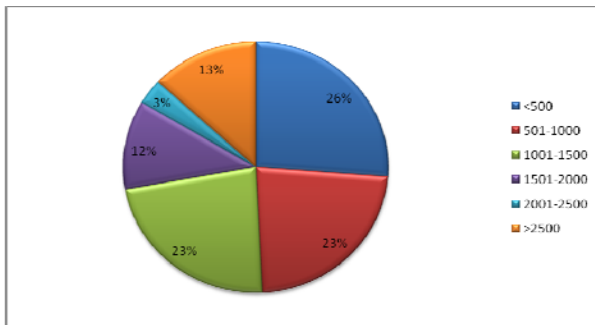
Fig.3. Viremia when starting treatment.

Viraemia average in women was 1.326 million ± 247,000 IU / ml and in men of 1.167 million ± 214,000 IU / ml.

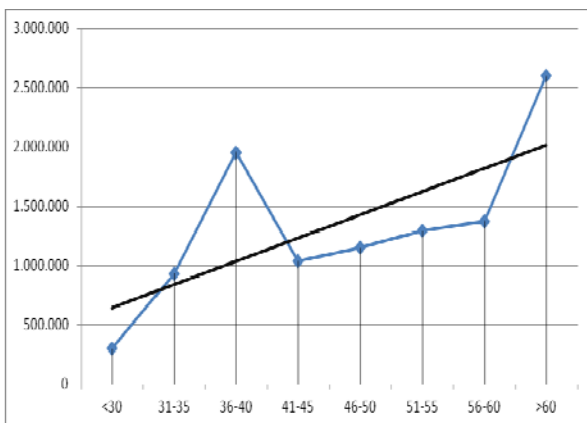By age group, viremia recorded the following tendency:

Fig. 4. Viremia average by group age.

There is a significantly higher viral load in women than in men (1326 to 1167). As expected, there is a directly proportional correlation of viremia with age. This is explained by the longer duration of illness in the elderly average, plus other possible liver aggressions of different nature.

Research of correlation between patient age, viral load, liver cytolysis and histological damage

We have tried to find a correlation between the viral load and the amount of cytolysis or histological damage.

It is noted that viremia does not influence the value of transaminases or Knodell score. This is demonstrated by the correlation coefficient between the two sequences of values, as follows:

Viremia (Ul/ml)	No. of subjects	ALT medium	Inflammation	Fibrosis
<500	32	74,0013	2,9375	2,25
500-1000	28	82,0964	2,85714	2,28571
1000-1500	28	114,929	3	2,28571
1500-2000	14	112,629	2,71429	2,14286
2000-2500	4	73,25	2,5	2,5
>2500	16	86,2463	3	2,125

	Correlation coefficient
Viremia- ALT	0,04757813
Viremia- inflammation	0,03515427
Viremia- fibrosis	-0,1179129
ALT- inflammation	0,09525411
ALT- fibrosis	0,27885291

This table shows a slight correlation in the positive (proportional) between hepatic cytolysis and histopathological damage.

Similarly we investigated the influence of the age factor on hepatic cytolysis, viral load and histological damage:

Age	Patients	ALT	Viremia	Inflammation	Fibrosis
<30	12	79	297.968	2,83	2,00
31-35	4	43	931.500	1,50	2,00
36-40	6	70	1.954.000	3,14	2,29
41-45	24	87	1.034.314	2,73	2,27
46-50	18	132	1.149.120	3,00	2,36
51-55	24	101	1.293.274	3,25	2,33
56-60	28	74	1.373.144	3,11	2,22
>60	6	77	2.599.219	2,33	2,00

The correlation coefficient for these rows of values calculated was the following:

	Correlation coefficient
Age- ALT	0,109
Age- viremia	0,262
Age- inflammation	0,141
Age- fibrosis	0,133

Age does not influence the amount of liver cytolysis (correlation below 0.3), but there is a strong correlation between patient age and viremia and between age and inflammation / fibrosis (coefficient> 0.8).

CONCLUSIONS

 Of the total patients who had received antiviral treatment two thirds were female.

 Numerical ratio between men and women varies by age, being almost equal before 40 years and over with increasing age.

 Initial viremia does not correlate with the amount of cytolysis or histological damage, but a higher value may influence response to treatment.

 Vast submitted is correlated with a higher viral load and a higher score of inflammation and fibrosis.

 Early viral response, accepted as a predictor for sustained response was present in 91 % of patients treated.

 The study showed a significant reduction of hepatic cytolysis after treatment and if at first the majority of patients have values 2-3 times upper limit of normal, after 6 months 77, 27 % had normal transaminases.

 Lack of a significant percentage of patients who do not respond early was an impediment in determining predictive factors for lack of response to therapy. However we found a better response in those with lower viremia and females.

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