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# CONSIDERATIONS REGARDING STRESS AND NEUROPSYCHIATRIC CHANGES IN PATIENTS WITH CHRONIC VIRAL LIVER DISEASES

## PHD THESIS

## ABSTRACT

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**CONTENTS:**

**INTRODUCTION**

Chronical viral liver disease  is a very complex health problem, uncompletely elucidated, involving numerous systems, including the nervous system. Studing this chapter from only one direction, just from the hepatologically point of view, is not enough. In the context of modern life, stress became something like a"daily banality". We cannot explain some of the psyshiological or pathological human conditions without refering to the stress influence.  We consider that the association between stress, liver disorders and mental illness represents one of the biggest challenges of modern pathology and I found it like a challenge for myself to study in my doctoral thesis.

**CURRENT KNOWLEDGE**

**1.CHRONIC HEPATITIS. GENERAL ASPECTS.NOSOLOGICAL CONTEXT**

**1.1 Definition:** By the term of chronic hepatitis we understand the presence of the  liver inflamation and necrosis for more than 6 months.

**1.2 Classification:**

Because the clasical classification of the chronic hepatitis reporting on histopathological criteria did not have a prognostical value, there was introduced another classification based on ethiologically criteria, necro-inflammatory activity and the extension of fibrosis stages.

**1.3 Pathogeny:**There is an immunological mechanism involved in liver agression, having the cellular substrat on the membrane of hepatocytes.

**1.4 Symptoms:** The clinical aspects of chronic viral hepatitis are common. Sometimes, the symptoms are not present. But usually, the patient has asthenia, digestive symptoms, pain on the right hypocondrium, myalgia and arthralgia.

**1.5 Paraclinical diagnosis:** It includes functional, imagistic, morphological, immunological and ethiological tests.

**1.6 Positive diagnosis:** It involves establishing the diagnosis of chronic hepatitis in order to specify the ethiology**.**

**1.7 Differential diagnosis:** It is necessary to make a differential diagnosis between the chronic viral hepatitis and cirrhosis, or other diseases like hemochromatosis or Wilson disease.

**2. MAIN MENTAL DISORDERS INVOLVED IN CHRONIC VIRAL HEPATITIS**

An early detection of psychiatric symptoms in chronical hepatitis is very important, especially during interferone therapy. The incidence of depression was between 22% and 59% in people suffering from viral C hepatitis and the incidence of depression is higher compared to the peolpe suffering from chronical viral B hepatitis.

The number of patients with chronic C hepatits and depressive disorder increased between 1995-2005 from 18% to 35 %.

**2.1 Mental disorders associated to somatic disease**

Psychiatric symptoms of somatic disease can take the aspects of psychiatric syndromes like cognitive, affective, anxious, psychotic or sleeping disorders. (according to Kurt Schneider quoted by Prelipceanu).

**2.2 Psychiatric symptoms in chronical hepatitis:**

Depression and anxiety have a higher prevalence in chronic viral hepatitis.

Depressive mood might be accompanied by symptoms like anhedonia, apetite changes, sleeping disorders, feelings of guilt or suicide behaviour.

**2.3 Some psychatric symptoms in infectious diseases. Infectious and fever delirium:**

We are speaking about periods of agitation accompanied by anxiety and oneiroid symptoms, delusions and episodes of depersonalization or changes of different parts of their body. All these symptoms appear in the period of fever.

**2.4 Mental disorders from portal-systemic encephalopathy**

Portal-systemic encephalopathy can be desribed by jaundice, ataxia, convulsion symptoms and flapping tremor.

**2.5 Considerations regarding stress**

It considered that there are two kinds of stress: positive stress and negative stress.

The negative part of stress is called distress. Distress disturbs the daily activity and sometimes becomes a negative factor for depression or anxiety.

On the other hand, the possitive stress is called eustress and it is a beautiful experience and very stimulative one. (T.Looker, Olga Gregson 2008)

**2.6:Considerations regarding mental changes after chronical hepatitis treatment**

The most common depresive symptoms presented in chronical hepatitis C, after antiviral treatment are depresive mood, astenia and suicidal behaviour.

**PERSONAL CONTRIBUTION**

**3. STUDY PURPOSE**

We proposed to study the correlation between stress and chronic viral hepatic diseases.

**4. PACIENTS AND METHODS**

The studied group included 124 patients hospitalized in the Clinic of Gastroenterology within the Clinical County Emergency Hospital of Craiova.

The research study was performed between January 1st and June 30th 2016.

The subjects included in our study underwent a complex examination, both clinically and paraclinically, in order to establish the diagnosis of chronic viral hepatitis, according to the present diagnosis criteria.

The subjects were asked to complete a questionnaire of 10 items regarding the stress felt every day and their activities in the last period of time. The patients were asked to answer by giving scores from 0 to 4 to every question.

***The statistic analysis:*** For the statistic analysis we usedMicrosoft Excel 2010 (Microsoft Corp., Redmond, WA, USA), with XLSTAT 2014 for MS Excel (Addinsoft SARL, Paris, France) and IBM SPSS Statistics 20.0 (IBM Corporation, Armonk, NY, USA).

**5. RESULTS**

**5.1 Age:** We can see that 11 subjects (8.87%) were between 40-49 years old, 27 pacients(21.77%) were between 50 and 59 years old, 54 subjects(43.55%) were 60-69 years old, 27 patients(21.77%)were 70-79 years old andjust 5 pacients(4.03%)were between 80-85 years old.

**5.2 Sex:** The incidence of women with chronical viral liver disease was higher comparing to the men with similar pathology. We identified 75 women(60.48%) and 49 men (39.52%).

**5.3Environmental origin:** Speaking about environmental orgin,70 persons(56.45%)came from the townand 54 (43.55%) came from the countryside.

**5.4 Job:** In our group study, the highest percent was represented by retired people.They were 94, (75.80%). The second highest percent was represented by the people without any job- 18 (14.52%). We count only 12 employees (9.68%).

**5.5　Marital status:**The highest percent is represented by married people 107 (86.29%), divorced and widows being just 17 (13.71%)

**5.6 Education level:** The highest percent of the patients graduated highschool (34 pacients-27.42%), 32  pacients graduated  a tehnical school (25.81%), 20 pacients(16.13%) graduated just eight classes and 28 (22.58%) graduated less than eight classes.

Only 10 subjects(8.06%) graduated a college.

**5.7 Alcohol :** Pacients was asked if they use to drink and we found that 31 pacients (25%) use to drink alcohol an 93 subjects(75%) denied this custom.

**5.8　Smoking:** In our group of patients we had 24 smokers(19.35%) and 100 people who don't smoke(80.65%).

**5.9 Cofee:** A number of 59 patients(47.58%)  declared that they use to drink at least one cup of cofee dailyau and 65(52.42%) denied it.

**5.10 Level of living:**

The evaluation of the level of living was made in a subjective way, we let the pacients to choose one of the group of stress: „low", „medium", „good", „very good"

A number of 23(18.54%) patients considered that they have a low level of living , 66 (53.22%) –medium level and around 35 person(28.24%) considered that they have a good or very good level of life.

**5.11 Level of stress:** A number of 35(28,23%) patients considered that they have a low level of stress, 61(49,19) a medium level of stress and 28(22.58%) thought that they have high level of stress.

**5.12 Diagnosis**: Most people from our research were diagnosticated with chronical viral hepatitis C-65 patients, 30 patiens have viral cihrrosis C, 18 patients-chronical viral hepatitis B, 6 pacients presented viral cirrhosis B, 3 patients -viral cirrhosis B+C, one  pacient was diagnoticated with chronical viral hepatitis B+Cand one with liver cirrhosis B+D.

**5.13The evaluation of the level of stres:**

We found scores between 0 and 10 at 6 patient, between 11 and 20 at 56 patients , between 21-30 at 61 patients and only one score between 31 and 40.

*5.13.1 Correlation between sex and level of stress:*

We identified a semnificant difference between men and women regarding stress evaluated by our questionaire . The result of Chi test ,p=0,030 <0,05, shows that women present a higher level of stress comparing with men.

***5.13.2Correlations regardind environmental origin and level of stress:*** Also, environmental origin presents a high signifiant statistical relation regarding level of stress, patient from the coutryside registering a higher level of stress comparing with the people from the town. (p Chi=0,0000066< 0,001).

***5.13.3 Correlations regarding the patient's job and level of stress:*** The occupational status of he subjects has a signifiant statistic impact over the level of stress, *(* p=0,029 <0,05). So, we can say that retired people registered are more stressed comparing to the other people from our study.

***5.13.4*** Correlations between the level of stress percepted by subjects and the level of stress evaluated by yhe questionaire: Generally, we found correlations between the level of stress felt by patients and the levele of stress evaluated by questionaire, but from the statistical point of view , the difference are not signifiant. (p Chi=0,246>0,05).

***5.13.5 Correlations between marital status and stress level:***

Marital status didn't present a signifiant influence over the level of stress evaluated by questionaire.p=0,849>0,05.

***5.13.6 Correlation between smoking and level of stress:***

Altought, there are theories saying that smoking has an anxiolytic effect, in our study this hypothesis wasn't confirmed.

***5.13.7 Correlations between alcohol and level of stress:***

Our study shows that the people who use to drink alcohol presented a lower level of stress as the people who don't use alcohol**.**The difference is not signifiant,the result beingp=0,119>0,05.

***5.13.8 Correlation between drinking cofee and the level of stress:***

We didn't identify a high difference for the people who drink cofee comparing with the people who don't use to drink cofee.

***5.13.9 Correlation between level of living and level of stress:***

The analyse of our results confirmed that the level of living is correlated with the level of stress. The pacient wiht a high level of living have a lower level of stress comparing to the others. (p Chi=0,020 < 0,05).

***5.13.10 Correlations regarding thee education level and the level of stress:***

Using statistical tests we showed that a low education level is corelated with high level of stressp=0,003<0,05.

*5.13.11Correlations between diagnosis and level of stress:*

*We considered that people who are suffering of cirrhosis have a higher stress level comparing with the people diagnosticated with hepatitis.*( p=0,029<0,05).

## 6. DISCUSSIONS

**6.1 Age:** The higher incidence of patients diagnosticated with chronical lviral liver disease affected by stress was registered between 60 and 69 years**.** It is possible that at this agetime , the period from the beggining of the disease and hospitalazation is long, the development of the stress being a negative factor for a mental illness. We considered that these persons have many factors of stress represented not only by the stress generated by the disease but also by the long period on monitoring based on a couple of investigation corelated with unsignifiant results and by the side effects of the treatment.

**6.2 Sex:** In our group we observed a relative signifiant disproportion between women and men.

Altoughboth the management of liver disease as the complication are quite similar at the men and at the women, there are still many differences based on sex and ethiology, on progression and the efficiency of the treatment.

**6.3 Environmental origin:**

Studing from the environmental point of view we can say that the biggest percent is represented by the patients from urban environment.(56.45%)

One of the reason of higher incidence at the patients from urban environmental may be the bigger adressability for the monitoring methods and modern terapies comparing to the people from countryside.

**6.4 Work:** Studying the group regarding the working place we observed that the bigges percent is represented by the retrees person (75.80%), followed by the person without job (14.52%) andthe employees (9.68%).

There is a logical distribution because the chronical viral liver disease is a disease which takes a long period of time with many episodes of remission and relapse.

Neuropsychiatric simptoms are more frequent at the older people diagnosticated with chronical liver disease.

**6.5 Marital status:**

The most patients from our group are married (86.29%) comparing with divorced people or widdows. (13.71%).

### 6.6 Level of education:

The biggest percent is represented by the patients with medium level of study (34- 27,42%).

Around 44(35.48%) patients have graduated a highschool or a college. This thing can be explained by the fact that the persons with a higher level of education can understand easier the preliminary symptoms of a eventually disease and they are learnt to go for a consult, but as the education level increases, there also improves the awareness of the disease, its related problems, and the complexity of the treatment represents a stress factor more intensely perceived by the patients with an average and high level education.

.**6.7 Alcohol intake:** By analysing the group regarding the alcohol intake, we state even from the beginning that the results are extremely subjective, a high number of patients where alcoholism has been or still is present avoid admitting they have this addiction, due to stigmatization or social and cultural convictions.

Still, the fact that 31 patients (25%) admitted that alcohol intake associated with liver disease is quite relevant in evaluating the risk for chronic alcoholism in the unfavourable progression of the liver disease, and also of the onset of mental disroders.

Chronic alcoholism is an anxiety and depression generator factor, and also chronic liver disease may generate effects belonging to the depressive spectrum. The simultaneity of the two entities favours the two entities, both regarding the severity of the liver disease and the mental disorder onset and progression.

**6.8 Standard of living:** The evaluation of the living standard was made in a subjective way, allowing the patients to choose the category they belong to.

A very exact analysis of this parameter included the existence of certain financial data, according to which the average family income should be known and confirmed. But also in the absence of this objective information, the simple personal evaluation of the standard of living in patients with chronic hepatitis and neuropsychological symptoms may be analyzed.

Our data showed that only 23 of the patients had a low standard of living (18.54%) and most of them presented an average and high standard of living.

6.9 **Subjective evaluation of stress degree**: In our study, we also included a subjective evaluation of the patinets reagrading stress, in general, and the one caused by the disease, in particular.

After analyzing the results, the conclusion was that 61 patients (49.19%) consider that they had an average stress level, and 28 patients (22.58%) a high stress level. Only 35 patients (28.23%) of the patients reported a low stress level.

There is no doubt that these patients are expected to admit the existence of certain significant psycho stressor factors that generate psychological changes in the context of chronic liver disease.

**6.10 Analysis of the study group in relation to the liver disease etiology and stress level:** The studied group was diagnosed with one of the chronic forms of viral hepatitis or cirrhosis in previous hospital admissions or at present admission.

We observed that most of the patients presented chronic C virus hepatitits or C virus liver cirrhosis (95 patients). There follow the ones with B virus hepatitis and liver cirrhosis (24 patients), and the ones with forms of B+C virus hepatitis or cirrhosis included only 5 cases.

**6.11 Evaluation of stress level:** The new distribution of patients according to the stress level showed that the values in the two groups are quite similar, and that high stress symptoms are as frequent as low stress symptoms.

Making a connection with the results from the previous analysis, we can state that there is a low number of patients with very high stress level or without any stress level, and that the percentage of liver disease and neuropsychological symptoms is mainly found in those with an average stress level.

*6.11.1 Sexul and living environment:* The statistical analysis of the group regarding the sex and living environment of the patients, without considering the stress level, showed that the majority was represented by women from the rural area. (60%).

*6.11.2 Sex and stress level:* By analyzing the sex of the patients correlated to the stress level, we identified a significant value (61.22%) in men from the low stress group. In the group of female patients, the low stress level was present in most of the patients (58.67%).

Thus, in the group studied by us, women were more stressed by the presence of liver disease than men.

*6.11.3 Living environment and stress level:* By analyzing the correlation between the living environment and stress level, the peak value is represented, paradoxally, by the patients with low stress level in the urban area (72.22%). Patients with a high stress level are more frequently found in the rural area (68.57%).

Our study analyzed the correlation between the living environment and stress level, and also the stress intensity (according to the questionnaire): low or high.

***6.11.4 Patients work place and stress level:*** By studying the correlation between the patients work place and stress level, we may state that the working patients are less stressed (75%). On the second place, we may find the non-working patients where the percentage of low stress level subjects is 66.67%. In the work group represented by retired people, the percentages invert, the majority of 57.45% belonging to those with a high stress level.

***6.11.5 The stress level perceived by the patient and the stress level evaluated by the questionnaire:*** Regarding the connection between the stress level felt by the patient and the stress level evaluated by the questionnaire, we observe clear correlations between the stated stress level and the one confirmed by the questionnaire.

***6.11.6 Marital status and stress level:*** The correlation regarding the marital status and stress level shows that the higher percentage is represented by single persons with high stress level (52.94%). Between this group and the group of married persons, the difference is a minimum one (52.94/ 50.46%), which shows that stress stress caused by viral liver disease is high both in the married ones and in the single persons.

***6.11.7 Smoking and stress level:*** Associating smoking with stress shows a slightly higher value above the average (51%) in the non-smoking group regarding the high stress level, in comparison to smokers in whom the two groups (high stress level/ limited stress level) are similar (50/50%).

***6.11.8 Alcohol intake and stress level:*** The correlation between alcohol intake and stress level shows a peak of 61.29% in low stress level persons not consuming alcohol. On the other side, in those frequently consuming alcohol, the balance inclines towards the patients with a high stress level.

Although alcohol is known as being a short-term anxiolythic and a long-term anxiogen factor, the minimum differences between the two groups show that the stress level is less influenced by the alcohol intake of patients with chronic viral liver disease.

***6.11.9 Coffee and stress level:***

The association between coffee intake and stress level shows unsignificant differences between those consuming coffee and those who do not consume it. In the group of coffee consumers, a relative percentage is represented by those with a high stress level (52.54%) in comparison to those who do not consume coffee, the stress level being significantly similar. The minimum unsignificant differences between the stress level of persons drinking/ not-drinking coffee and have a liver disease with a chronic evolution show that both the anxiolythic and activator effects of coffee are still controversial.

*6.11.10 The patients standard of living and stress level:* By analyzing this correlation, we observed that the most stressed are the patients with an average standard of living and not those with a low standard of living, as expected. The lowest stress level was found in the patients with high standard of living, this confirming the fact that material resources represent an "anxiolythic factor" in the patients with chronic liver disease.

*6.11.11 Educational level and stress level:* Opposed to our expectations, the percentage with high stress level persons belongs to those who have a low or relatively low educational level. As the educational level increases, the stress level is getting lower, in highschool graduating persons being observed a low stress level in 67.65% of patients.

This observation seems paradoxal, as our expectations were that stress increases directly proportional with the educational level.

*6.11.12 Liver disease and stress level:* The study of the correlation beween viral liver disease and stress level shows that the most stressed are the patients with cirrhosis, where the high stress percentage represents 65% compared to those diagnosed with chronic viral liver disease, who recorded a percentage of 44.05%. These results were predictable, as cirrhosis is a more serious disease, with a prolonged progression, sometimes with an unfavourable prognosis, with significant complications, which may lead to a high stress level in these patients.

## 7.    CONCLUSIONS

➢    *Chronic viral liver disease was mainly identified in the patients aged between 60-69 years old (43.55%), more frequently in women (60.48%), in patients of the urban area (56.45%), retired persons, married persons with an average educational level (27.48% highschool graduates.*

➢    *Most of the patients diagnosed with chronic liver disease confirmed the alcohol abstinence by 75%, they declared as non-smokers – 80.65%, no coffee consumption 52.42% and they mentioned an average standard of living in a percentage of 53.23%.*

➢    *Our group of patients perceives an average stress level in a percentage of 49.19%, as patients with chronic viral hepatitis represented the majority (67.74%) in comparison to those with viral cirrhosis (2.26%).*

➢    *The objective evaluation of stress level was esatblished by a questionnaire revealing unsignificant differences between high stress level patients (total score>20) -50.81% in comparison to those with a score lower than 20, representing 49.19%.*

➢　*The correlations made based on this qustionnaire showed that an excess stress is found in women of rural areas, in retired persons in comparison to working or not-working persons 57.45%, in the patients that declare a high stress level 60.71%, as well as in the single persons 52.94%.*

➢　*The stress declared by the patients was slightly higher in non-smokers 51.51%, in those not consuming alcohol 54.84%, as well as in those consuming coffee 52.54%.*

➢　*The patients with chronic liver disease and low stress level are those who have a high and very high stress level, with highschool or academic studies.*

➢　*The patients diagnosed with chronic hepatitis present a lower stress level in comparison to those suffering from chronic cirrhosis.*

➢　*Our study showed that stress represents an extremely important element in the analysis of chronic liver disease implications over the human mind.*