

Mental Disorders in Chronic Liver Diseases with Viral Etiology

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ABSTRACT: The study of chronic viral hepatitis represents a real challenge for modern medicine. If we also analyze this illness from the point of the mental changes involved, the complexity of the study increases. To the etiological, symptomatological polymorphism, alongside the paraclinical and conduct diagnosis, there may be easily added the multitude of mental disorders. The authors have tried, through this paper, to draw the attention upon the importance of studying certain mental disorders connected to a somatic disease, each and every representing a distinct entity, but which together may reach a remarkable complexity.

KEYWORDS: chronic hepatitis depression, psychosis

Introduction

By chronic hepatitis, one understands the presence of liver inflammation and necrosis for at least 6 months.

Histopathologically, clinically and biologically speaking, they represent common features of chronic hepatitis, no matter if these succeed an acute viral, autoimmune or drug-induced hepatitis. Besides these, there are chronic hepatitises that do not enter any of the previously mentioned categories, being a form of "idiopathic" chronic hepatitis.

Regardless of the etiopathogenic form, the evolution of these chronic hepatitises varies from mild forms, with slow progression, up to severe forms, with fibrosis and architectural disarrangements that will subsequently determine hepatic cirrhosis [1].

The criteria according to which a mental disorder associated to a somatic disease could be included in this category are the following:

- to be the etiopathogenic consequence of a diagnosed somatic disease
- not to be caused by another mental disorder
- not to comply with diagnosis criteria for dementia
- not to be caused by the use of psycho affective substances
- not to emerge only in the case of a conscience disorder (delirium)[2]

Objectives

Relatively recent data present in a statistical way the impact of the infections caused by

various viruses world widely, thus being estimated that there are 550 million people infected with hepatitis viruses, from which 350-400 million with hepatitis B virus, 170-180 million with hepatitis C virus and 15 million with hepatitis D virus. [3]

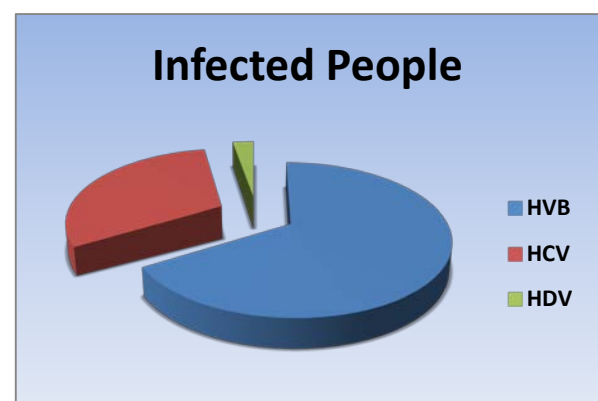


Fig.1. People are infected worldwide with hepatitis (Lemoine M.2014)

There is estimated that hepatitis viruses are present in 60% of the cirrhosis cases and 80% of the hepatocellular carcinoma cases. [3]

Depression represents a major problem for the public healthcare system. According to the Health World Organization, depressive disorder is the fourth cause of disability and will become, in 2020, the second cause, after cardiovascular diseases. [4]

Major depressive disorder more frequently starts between 20 and 40 years old, it is more frequent in women than in men, and old age presents a high risk for recurrences and suicidal tendencies. [4]

The characteristics of mental disorders caused by a somatic disease are:

- onset after the age of 40 years old
- simultaneous onset with a major somatic disease
- onset in a patient with a recorded history of mental disorders
- Patients that abusively use psycho active substances or those practicing self-medication.
- Persons in which the neuropsychiatric treatment was not efficient enough.
- There are heredo-collateral history of degenerative or metabolic diseases
- The mental clinical symptoms are represented by conscience disorders, fluctuant mental status, signs of cognitive deterioration, hearing, tactile or gustatory hallucinations.
- At general clinical examination there appear signs of dysfunction at the level of some organs, such as neurological focal signs, cortical dysfunction or sphincter incontinence.[2]

Methods

Our study was performed between 1.01.2014-31.12.2014 in Psychiatry I Department, from Craiova Clinically Hospital of Neuropsychiatry. We followed 52 patients diagnosticated with chronic hepatitis with viral etiology who presented also different psychiatric symptoms. At a number of 40 patients was identify the HBs antigen and at 12 patients anti-HCV.

Table 1. Patients diagnosticated with chronic hepatitis with viral etiology

	Cases	Percent
HBs atg.	40	76,92%
Anti HCV atb.	12	23,08%
Total	52	100,00%

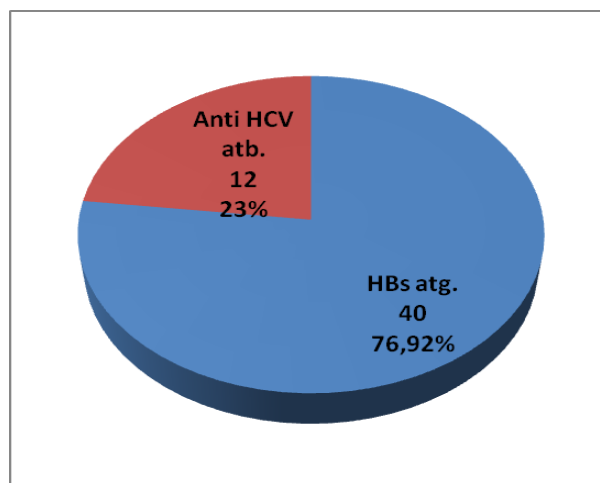


Fig.2. Patients diagnosticated with chronic hepatitis with viral etiology

Results

In our research, from 52 cases of patients with chronic hepatitis we identified 21 patients with anxiety symptoms and at 11 patients we found depressive symptoms. At two patients, the psychiatric disease was represented by psychotic symptoms and at 8 patients the psychiatric manifestation represented a cause of alcohol abuse. A number of 10 patients with chronic hepatitis benefit from interferon treatment and they presented psychiatrically disorders after interferon therapy.

Table 2. Psychiatric symptoms from patients with chronic hepatitis

Symptoms	Cases	Percent
Anxiety	21	40,38%
Depression	11	21,15%
Psychotic	2	3,85%
Substance abuse	8	15,38%
Post IFN therapy	10	19,23%
Total	52	100,00%

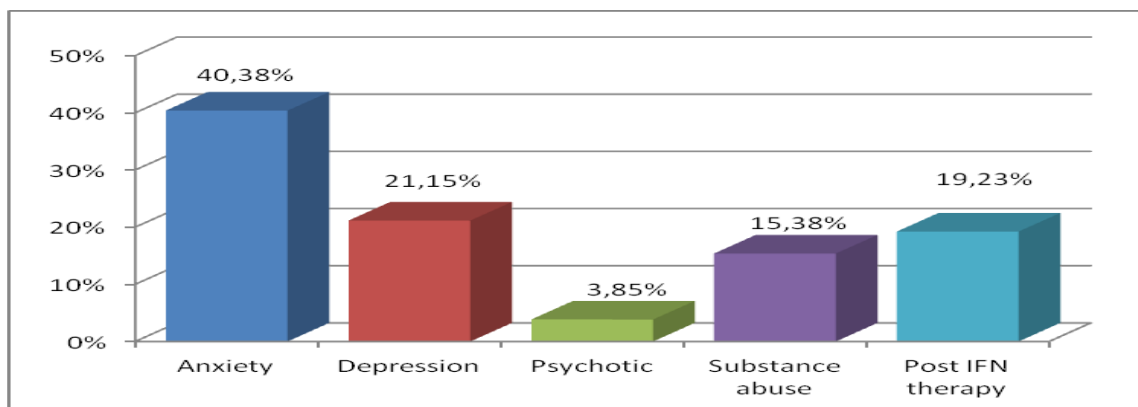


Fig.3. Psychiatric symptoms from patients with chronic hepatitis

Our group of research was made by a number of 30 patients who were at the first hospitalized and 22 patients had a lot of staying in psychiatric hospitals.

Table 3. Patients by number of hospitalizations

	Cases	Percent
First admission	30	57,69%
Multiple admissions	22	42,31%
Total	52	100,00%

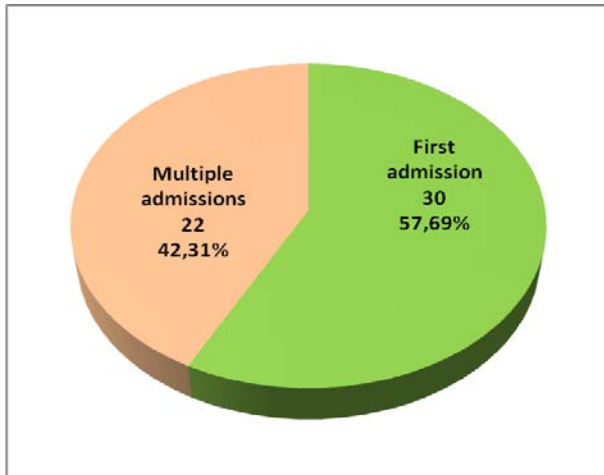


Fig.4. Patients by number of hospitalizations

A number of 33 patients benefited from psychiatric medication before hospitalized.

Table 4. Patients who received psychiatric treatment

Treatment	Cases	Percent
Previous treatment	33	63,46%
Without treatment	19	36,54%
Total	52	100,00%

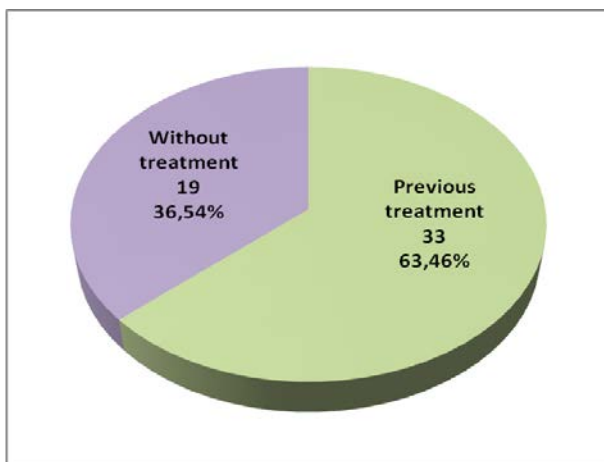


Fig.5. Patients who received psychiatric treatment

Because the patients were hospitalized in Psychiatry Department, the diagnosis of chronic hepatitis and the evidentiatio of hepatic fibrosis were established before hospitalized.

Discussions

The American College of Gastroenetrology established new guidelines, based on evidence connected to the diagnosis and management of liver lesions.

This evaluation is based on the ever growing use of several objectivation methods regarding liver lesions, such as echography, computer tomography and magnetic resonance that allowed the lesion detection in some patients with no clinical symptoms. [5]

Although most of liver focal lesions are benign, it is difficult to differentiate them from the malignant ones, or, in other words, it is difficult to establish whether some benign focal lesions do not also include a real malignant potential. [5]

The USA National Study for Health and Nutrition appreciated that there were 2.3 million persons chronically infected with hepatitis C virus at the beginning of 2013, in comparison to 3.2 million in 2001. The significant decrease of these values is mostly due to the implementation of a screening for detecting this disease, and, also to a really efficient treatment. Still, the modern methods of treatment, even though safe and without any side effects, present the disadvantage of being extremely expensive. [6]

Chronic C virus hepatitis is responsible for 350,000 deaths every year, both in persons with no clinical symptoms and in those who have a late advanced diagnosis of liver disease. Even in persons who receive an early treatment, this may prove inefficient and with negative side effects. Nevertheless, the absence of treatment offers a considerable morbidity, the evolution being to cirrhosis and hepatocellular carcinoma. Among the patients with chronic C virus hepatitis, approximately 20% develop cirrhosis after 20 years of infection. [7]

The etiological classification of chronic viral hepatitis is based on the existence of some criteria that individualize them: sex, prevalent age etiological associations, specific diagnosis tests, the possibility of progressing to cirrhosis and/ or hepatocellular cancer. treatment [1]

The clinical shades related to the etiology of chronic viral hepatitis are relatively reduced, the symptoms being more or less the same.

Undoubtedly, there is a chronic viral hepatitis without any clinical symptoms. When there are symptoms, they include the following:

- Physical asthenia. It is the most constant symptom of chronic viral hepatitis.
- Dyspeptic complaints (nausea, anorexia).
- Painful discomfort in the postprandial right hypochondrium or at effort.
- Myalgias
- Arthralgias

After the objective examination, we could observe an enlarged liver associated with an enlarged spleen. In chronic hepatitis, the liver has a normal or slightly increased consistence, a smooth surface and it is sensitive to palpation. Also during the clinical examination, we may observe jaundice or signs of severe liver failure (vascular stars, nose or gum bleeding) [1]

Chronic B virus hepatitis is characterized by the presence of inflammation “flares” under a continuous rate that may lead to fibrosis. The persistence of viral replication, as well as the onset of liver fibrosis may lead to cirrhosis and its complications, reason for which the identification of a fibrosis evaluation method becomes compulsory. Moreover, this fibrosis evaluation may be a marker for treatment monitoring. [8]

Highlighting liver fibrosis represents a criterion regarding the prognosis of liver disease and its treatment. Adding some seric markers (E,L,F) to the information obtained by transient elastography allowed increasing the performances upon the detection of liver fibrosis. [8]

A proper evaluation of the liver fibrosis stage is quite important. Not so long ago, the histopathological examination was considered to be the single evaluation method for this type of fibrosis. Nevertheless, liver biopsy, an invasive diagnosis method, was not embraced by all physicians, due to its risks, reason for which there were produced other methods, such as vibration transient elastography. It is a method based on ultrasounds that reveals the structure of liver tissue. [9]

This method has the following advantages:

- It is relatively easy to perform, technically speaking, having a great reproductivity
- It is a non-expensive and no side effects method
- It properly evaluates the stage of liver fibrosis
- It is useful not only for the patients with chronic C virus hepatitis, but also for other liver diseases

-Highlighting a high degree of liver rigidity may be a predictive factor for some severe illnesses, such as the hepatocellular carcinoma. [9]

There is a multifactorial theory, mainly connected to the neuro-immuno-endocrine triade, that attempts to explain the pathogenic aspect of depression, in general, and especially of depression in chronic viral hepatitis.

The history on depression marked an important moment when there was postulated the idea according to which the noradrenergic deficit at limbic level represents the essential mechanism in triggering depression (Bunney W.E. 1965) [4]

Subsequent research confirmed that mental disorders have a biological cause, being known the fact that there exists an interrelation between the levels of serotonin, noradrenaline, dopamine, acetylcholine, etc and depression. [4]

In depression, there appear immunological alterations affecting the T suppressor and T helper lymphocytes and also the lymphokine-secretion inhibiting process.

There is a direct relation between stress and depression. Stress itself activates the hypothalamic hypophysary suprarenal axis, having as a consequence the stimulation of the sympathetic system. There are opinions according to which the etiopathogeny of depressive disorders has a monoaminergic, neuroendocrine and immunological determination. [4]

There may be present mental disorders of the psychotic, affective, anxious, confusiv-delirious, amnestic, sexual dysfunctioning or sleep disorders type, in various somatic diseases: tumors, traumas, infections, epilepsy.

Also, there may appear a catatonic syndrome and personality disorders induced by a somatic disease or by syndroms of a somatic disease. [2]

Based on the data on magnetic resonance and spectroscopy, there was suggested the idea that there may be possible the presence of an encephalitis in the patients with C virus hepatitis, similar to the one described in the HIV patients.

The patients with chronic C virus infection, with problems of the cognitive functions, especially at the level of primary attention and executive function, may present high levels of anxiety and depression. [10]

There may also be observed paraclinical alterations, such as EEG alterations, whose path is slower in the patients with chronic C virus infection. Also, there was highlighted a low

level of the N-acetylaspartate/ creatinine level in the cerebral context in the spectroscopy determinations. [10]

All these alterations demonstrate that chronic C virus infection affects brain functions and their consequence is the occurrence of neuropsychic alterations.

The psychiatric diagnosis in somatic diseases may embrace the aspect of some multiple mental syndromes (after Kurt Schneider, quoted by Prelepceanu):

-Cognitive syndromes: organic delirium, organic amnesic disorder, dementia syndrome

-Schizophrenic disorders: organic psychotic disorder

-Affective disorders: organic affective disorder

-Anxious disorders: organic anxious disorder

-Sexual disorders: organic sexual dysfunction

-Organic sleep disorders.

A diagnosis differentiation of a mental disorder in the context of a somatic disease requires a most complete anamnesis, where the psychiatric interview is the last stage of any patient examination where there exists the supposition regarding some mental disorders in the context of an organic disease. [2]

The main mental signs and syndromes observed in organic mental pathology are the following:

1.Cognitive, anamnestic and operational disorders of thinking: perseveration, anterograde amnesia, voluntary attention diminishing, fixing amnesia, consecutive to attention disorder, loss of ideative flexibility, vocabulary reduction, etc.

2.Conscience alterations, such as night confusion, agitation, violence or motivational delirium episodes

3.Personality alterations: uninhibited, impulsive or apathic behaviour, suddenly interrupted by acute heteroaggressive bursts.

4.Visual hallucinations in delirium tremens, in the context of anxious conscience disorder.

5.Emergence of an anxious and unstable depressive mood, depression being the latest clinical manifestation in terminal illnesses. [2]

Cerebral manifestations of the infection

Approximately 50% of the patients with chronic C virus hepatitis may present asthenia and memory disorders. We may also find depression, attention and concentration problems, mixed insomnias, anxiety and irritability. These symptoms are relatively more frequent in chronic C hepatitis than in other liver diseases. [10]

It is possible that these neuropsychic manifestations could be independent of the virmia level. The pathology of these manifestations is not completely known. It is possible a direct effect of HCV upon the central nervous system. Sometimes, the virus persists in the organisms, in some organs and tissues where the immunological defence “does not have any access”. [10]

Some mental disorders in infectious diseases. Fever and infectious delirium

There are episodes of conscience deterioration of the delirium type in infectious diseases involving fever. They are more accentuated in the morning and evening, when there are morning or vesperal fever flares. There appear episodes of psychomotor agitation with critical anxiety and oneroid signs, with visual pathological hallucinations and visions, with akinetic mutism, episodes that appear when there is an important thermic ascending. The patient may have episodes of depersonalization, derealization or changes of body outline.[2]

The periods of fever delirium may be followed by lacunar amnesia and may mask the development of an infectious process, with cerebral localization, a reason for which it is required a careful neurological examination of the patient.

The infectious delirium overposes the fever delirium, but evolves independent of the fever, the latter being capable of exacerbating it. The infectious delirium usually accompanies cerebral infectious complications. [2]

There exists an interdependence between the hypothalamic-hypophysary-suprarenal axis, as well as between the thyroid-parathyroid system and the inflammatory response in chronic hepatitis. This interdependence is in direct relation to the serotonin level. Cytokines, in their turn, as a consequence of the inflammatory reaction produce alterations of serotonin receptors and tryptophan (a serotonin precursor), which explains the connection between the existence of a depressive disorder and chronic viral hepatitis. To these changes we may add anomalies of cerebral monoamines, with a depressive effect, a consequence of the antiviral medication. [11]

The part played by the biological systems in depression etiopathogeny, as well as the interrelations between somatic diseases and depressive disorder, are not sufficiently known, but it is well-known the fact that in chronic viral hepatitis mental symptoms have a high prevalence. [11]

Mental disorders in hepatic-portal encephalopathy

Hepatic-portal encephalopathy may clinically manifest through jaundice, ataxia, confusion, lack of coordination, liver foeter, as well as flapping tremor.

These signs and symptoms may be accompanied by mental signs. The most frequent and common ones are the diminishing of cognitive sensibility – an early sign that subsequently progresses towards mental slow-down, decrease of attention focus, irritability, reverse of wake-sleep span, sleepiness, transient disorientation, confusion, agitation. [2]

Liver encephalopathy is a manifestation of liver chronic failure, it is a generic term comprising a series of neuropsychic symptoms that may be found in the patients with acute or chronic viral hepatitis.

Usually, the symptoms emerge in the presence of some portal-systemic shunts that characterize liver cirrhosis.[12]

Mental disorders in liver transplantation

The patients that are on a waiting list for liver transplantation may suffer from accommodation changes during the preliminary stages, as well as the general stages and long-term accommodation stages to after-transplant life. [2]

There appear mental changes that require diagnosis and, sometimes, treatment.

The psychiatric examination when deciding to perform a liver transplantation is necessary in order to establish the patient's mental competence of giving a generally valid consent.

The same objectives should also be followed in the psychiatric evaluation of liver donors.

In the case of patients with a significantly high psychosocial risk (alcohol addiction), there are necessary additional interventions for the patient to comply with the selection conditions for transplantation.

The candidate-patients for a liver transplantation present a high risk of developing mental symptoms and disorders, such as mood disorders and anxiety, alongside cognitive dysfunctions and delirium.

Comorbid mental disorders interest about 40% of the patients with advanced liver disease.

After the transplant, approx. 30% of the patients develop mental disorders, especially in the first year after transplantation.[2]

The onset of anxiety and depression, before the transplantation, require an early psychotherapeutical intervention. Apathy, anhedonia, ideas of uselessness, of incurability, cognitive disorders represent a predictive factor

for a negative mental evolution and prognosis after transplantation.

There should be taken into consideration the fact that some of the symptoms of psychotic disorder are part of the symptoms of an advanced stage of the disease for which the transplantation was performed (portal-systemic encephalopathy)[2]

An insufficiently solved problem is the one of substance addiction, such as alcohol, in the persons that will suffer a liver transplantation. There has been suggested that there should exist an abstinence period of six months before the transplantation, but it is possible that during this period, the liver disease might considerably aggravate and the period could last longer.[2]

Conclusion

There exists a polymorphism of symptoms in chronic viral hepatitis, but the same polymorphism is observed in mental disorders caused by some somatic diseases. Due to a significant incidence of mental changes in chronic viral hepatitis, it is required a study involving all their aspects. The complexity of mental co-affection over poses on the etiological, clinical, diagnosis and therapeutical complexity of chronic viral hepatitis.

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