Hepatitis C has been associated with extra-hepatic manifestation of autoimmunity, which is expressed by the presence of non-organ specific autoantibodies and mainly cryoglobulinaemia in the patients. In this paper, we review some of these autoimmune aspects using as a reference Brazilian HCV carriers living in the state of Bahia.

Key words: hepatitis C, autoimmunity, cryoglobulinemia, autoantibodies, Brazil.

Hepatite C tem sido associada com manifestação extra-hepática de autoimunidade, a qual é expressa pela presença de autoanticorpos e principalmente crioglobulinemia nos pacientes. Neste artigo, nós revisamos alguns destes aspectos autoimunes, usando como referência portadores de infecção pelo virus da hepatite C, residentes no Estado da Bahia.

Palavras-chave: hepatite C, autoimunidade, crioglobulinemia, autoanticorpos, Brasil.

Hepatitis C is a global public health problem, presenting an estimated prevalence of 2.2-3% worldwide (130 - 170 million people), varying in Brazil from 2.5-10.0%\(^6\).

Hepatitis C virus infection provokes dysfunction in B-lymphocytes with extra-hepatic manifestations of autoimmunity, which have been well documented in chronically infected patients by the presence of non-organ specific autoantibodies and cryoglobulinaemia, which is the most important expression of autoimmunity in HCV carriers. It is provoked by a cryoprecipitable immune complex formed by polyclonal or monoclonal anti-IgG autoantibodies (rheumatoid factor, RF), which are more frequently IgM antibodies that react with the constant region of IgG antibody bound to HCV antigen plus complement C1q. Cryoglobulins can cause purpura, vasculitis, glomerulonephritis and peripheral neuropathy. Higher level of cryoglobulinaemia has been found in HCV carriers with lymphoproliferative disorders, mainly B-cell non-Hodgkin lymphoma\(^7,8,10\).

In a study performed with Brazilian HCV carriers living in the State of Bahia, mainly Afro-descents without a clinical history of HCV infection associated with the illicit use of injectable drugs, cryoglobulinaemia was found in about one-half of these individuals. Interestingly, vasculitis or glomerulonephritis were rarely documented in their medical files\(^6\).

The presence of non-organ specific autoantibodies is another expression of autoimmunity found in HCV carriers, which has been associated in some studies with advanced fibrosis and failure in the treatment of hepatitis C with the combined therapy of interferon-á plus ribavirin\(^13,15\). Antibodies to self-antigens as nucleoproteins (ANA), smooth muscle (SMA), liver-kidney microsomal type-1 antigen (LKM-1), immunoglobulin G (RF), neutrophil cytoplasm (ANCA) and phospholipids (APL), which are routinely used as biomarkers of autoimmune diseases, can be found in HCV-carriers with varied prevalence. Their induction seems mainly to involve immune crossed-reactions caused by molecular mimicry between HCV polyprotein and human autoantigens, as demonstrated by structural homology studies using viral synthetic peptides and immunoassays with sera from children chronically infected with HCV\(^4\).

Untreated Brazilian HCV-carriers have autoantibodies against several of these autoantigens, which present varied prevalence. The most prevalent autoantibody in these subjects is IgM-rheumatoid factor, which is associated with cryoglobulinaemia. Antinuclear antibodies may be detected in about one-quarter of these individuals, but only in a few seropositive HCV-carriers their immune specificity have been identified, which have been associated with the immune recognition of the 52 kDa isoform of the ribonucleoprotein SS-A/Ro. Anti-dsDNA autoantibodies, which are biomarkers of systemic lupus erythematosus and may also be found in autoimmune hepatitis, have not been found in this population\(^1\).

Moderate titters of anti-â2-glycoprotein I (â2GPI) IgM antibodies and mainly moderate-to-high titters of IgA antibodies against this coagulation co-factor were also found with significant prevalence in these individuals, confirming previous reports showing higher IgA-APL seropositivity in Afro-descents. Anticardiolipin IgM antibodies with low-to-moderate titters may be also found in these subjects, whereas both cardioliþn IgG and IgA antibodies are rarely detected in significant titters. Nevertheless, no clinical manifestation of antiphospholipid syndrome (APS), including thrombocytopenia, stroke, and neither venous nor arterial thrombosis have been found in these Brazilian HCV-carriers\(^13\). Smooth muscle antibodies were found in low titters in about one-third of these patients, but LKM-1 and mitochondrial autoantibodies. Absence or very low prevalence of LKM-1 autoantibodies has been also reported in HCV carriers of North America origin and contrasts with the high prevalence of these
autoantibodies in Italian and French HCV-carriers\textsuperscript{9).} Such findings clearly demonstrate the role of genetic background and ethnic factors in the expression of some autoimmune markers during the chronic infection caused by HCV.

In conclusion, the studies on autoimmunity in Brazilian HCV carriers should contribute to the better understanding of the immunopathogenesis of the chronic HCV-infection in Brazil, improving the clinical management and treatment of hepatitis C in the public health services in this country.

References