doi.org/10.1590/S0004-2803.202203000-59

The evolving field of hepatology in Brazil

Bittencourt PL. The evolving field of hepatology in Brazil. Arq Gastroenterol. 2022;59(3):325-6.

Management of patients with liver diseases has evolved dramatically in Brazil in the last decades with the incorporation of several evidence-based recommendations in routine clinical practice. Most of those recommendations, endorsed by the Brazilian Society of Hepatology, were published as position papers or guidelines in different issues of **Archives of Gastroenterology**[1-8].

Until recently, hepatitis B and C were the leading causes of end-stage liver disease and the most common indication for liver transplantation (LT) in Brazil[9]. However, this scenario is rapidly changing due to the emergence of non-alcoholic fatty liver disease (NAFLD) and alcoholic liver disease (ALD) in recent years in association with a parallel decrease in the burden of viral hepatitis in the country as a consequence of:

1) implementation of universal hepatitis B vaccination for all age groups.

2) achievement of hepatitis B virus suppression with high genetic barrier nucleotide analogues such as entecavir, tenofovir disoproxil fumarate and recently tenofovir alafenamide.

3) hepatitis C virus cure with the use of highly effective direct acting antivirals (DAAs).

Worldwide elimination of hepatitis C is now feasible[10] as a result of the wide distribution of point of care rapid hepatitis C virus tests and pangenotypic DDAs regimens, which are nowadays available, even in remote regions of the country. It is worth to mention that Brazil is indeed in a vantage position for viral hepatitis elimination when compared to several other nations, since all steps of the cascade of care of hepatitis B and C are entirely covered by the Unified Health System (SUS).

The country also ranks 2nd worldwide in the number of LT procedures performed per year with outcomes similar to those reported in Europe and the United States[9]. In spite of those figures, mortality due to cirrhosis and mortality in the LT waiting list is unacceptably high in Brazil, due to the occurrence of several barriers in provision of healthcare for patients with cirrhosis. Other frequently neglected liver diseases in the country are ALD, now the leading cause of mortality attributed to alcohol consumption in the Brazil[11], drug-induced liver injury (DILI), often caused by over the counter complementary and alternative medicine (CAM) compounds and carcinoma hepatocelular (HCC), which is often diagnosed in late stages, when the tumor is not amenable to treatment modalities known to increase patient survival[12]. Our preparedness index for tackling NAFLD was also considered to be suboptimal by an international panel of experts[13] in face of its expanding burden linked to the pandemic of obesity and type 2 diabetes (T2D).

New frontiers have been also opened for hepatology practice in the multidisciplinary approach to metabolic syndrome, T2D and obesity; organ transplantation; obstetrics; oncology and critical care medicine. Experimental, translational and clinical research in this evolving field has also increased exponentially in recent years, extending the number of scientific publications in the literature as a result of the recent launching of several high-impact journals entirely devoted to hepatology research. It was therefore not surprising to disclose in the present issue of **Archives of Gastroenterology** so many articles addressing different topics on this field. Interestingly, none of them dealt with viral hepatitis. Instead, in this issue of **Archives of Gastroenterology**, Barreto et al.[14] evaluated retrospectively Brazilian subjects with NAFLD and found that HOMA IR values could identify subjects more prone to develop advanced fibrosis or cirrhosis. The authors suggested that HOMA IR could be a valuable tool to identify those patients with non-alcoholic steatohepatitis, but prospective validation and comparison of HOMA IR with other readily available non-invasive markers of fibrosis in the Brazilian population is still an unmet need. Fernandes Ferreira et al.[15], on the other hand, have investigated serum and gene expression of several markers of angiogenesis and cell differentiation in subjects with HCC. The authors have correlated overexpression of vascular endothelial growth factor and alpha fetoprotein in liver tissue of subjects with HCC, particularly in those with advanced stages according to BCLC classification. Until recently[16] few Brazilian centers were accepting HIV+ patients for LT due to stigma and fear of adverse postoperative outcomes. Hyppolito et al.[17] have described the follow-up of HIV+ subjects after LT with outcomes very similar to those reported in patients without HIV, supporting the widespread notion that HIV status per se should not withhold LT whenever indicated. Malnutrition and sarcopenia are frequently encountered in patients with cirrhosis, even in those with compensated liver disease. Rossi et al.[18] have conducted a randomized controlled, parallel, open-label, clinical trial comparing a face to face supervised moderate exercise program to home-based moderate exercise without face to face supervision in a small cohort of patients with compensated cirrhosis. The former group of patients had better outcomes when compared to their counterparts randomized for home training. Those results reinforce the importance of physical activity in the management of patients with cirrhosis to prevent malnutrition and frailty. Oliveira et al.[19] have reported that quite half of those patients with pre-eclampsia and eclampsia have abnormal liver enzymes when admitted to the ICU, usually outside the spectrum of HELLP syndrome. Maternal and fetal mortality was negligible and few have developed life-

threatening liver related complications. Garg et al.[20] have described their results with the use of cyanoacrylate glue in patients from India with bleeding gastric and esophageal varices. Hemostasis was achieved in all subjects but the reported 6-week mortality was higher than expected. The authors made no comments regarding the employment to standard of care recommendations for the management of variceal bleeding in those patients[7] beyond endoscopic treatment. It is therefore possible that non-adherence to strategies known to improve survival could be a plausible explanation for the suboptimal reported 6-week outcomes. One interesting report concerning high prevalence of CAM use in subjects with inflammatory bowel disease was also published in the present issue of **Archives of Gastroenterology** by several investigators from São Paulo and Rio de Janeiro[21]. It is well known that approximately 1/3 of those patients with inflammatory bowel disease (IBD) have abnormal liver enzymes at least once in their lifetime, mainly due to hepatotoxicity usually attributed to the use of azathioprine, mercaptopurine, mesalazine, methotrexate, immunobiologics and even steroids. It is worth to mention, however, that several CAM compounds are now recognized as emergent causes of DILI or herbal induced liver injury[22]. Therefore, the reported prevalence of CAM users among IBD patients in Brazil should encourage physicians to screen actively the use of CAM compounds in every patient with IBD with signs or symptoms of hepatotoxicity.

In summary, the epidemiology of liver disease in Brasil is rapidly changing. Sooner than expected, NAFLD, ALD and DILI will turn out to be the major challenges in the field of hepatology, but new data, from several different groups of Brazilian investigators, are being published to improve the management of our patients with liver disease, as the reader would perceive in the following pages of this issue of **Archives of Gastroenterology**.

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Bittencourt PL. O emergente campo da hepatologia no Brasil. 2022;59(3):325-6.

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