A dual point-of-care test strategy to identify treatment-eligible hepatitis B virus patients in Africa

Authors:
Delil M[3], Desalegn H[3], Berhe N[4,5], Howell J[6,7,8,9], Johannessen A[10,11], Aabakken L[11,12], Van H[6], Anderson D[6,13], Bhat P[1,2].

[1]College of Health and Medicine, Australian National University, 2601 Canberra, Australia, [2] Gastroenterology and Hepatology Unit, Canberra Hospital, 2605 Canberra, Australia, [3] Department of Internal Medicine, St. Paul's Hospital Millennium Medical College, 1230 Addis Ababa, Ethiopia, [4] Aklilu Lemma Institute of Pathobiology, University of Addis Ababa, 1230 Addis Ababa, Ethiopia [5] Regional Centre for Imported and Tropical Diseases, Oslo University Hospital, Ulleval, Norway, [6] Disease Elimination, Burnet Institute, Melbourne, Australia, [7] Dept Gastroenterology, St Vincent's Hospital Melbourne, [8] Dept Medicine, University of Melbourne, [9] Dept Epidemiology and Preventive Medicine, Monash University [10] Faculty of Medicine, Institute for Clinical Medicine, University of Oslo, 0315 Oslo, Norway, [11] Department of Infectious Diseases, Vestfold Hospital Trust, 3103 Tønsberg, Norway, [12] Section for Gastroenterology, Department of Transplantation Medicine, Oslo University Hospital, Oslo, Norway, [13] Nanjing BioPoint Diagnostic Technologies, Nanjing PR China

Background: Antiviral treatment of chronic hepatitis B virus (HBV) infection reduces the risk of cirrhosis and hepatocellular cancer. International treatment criteria for HBV include elevated alanine transaminase (ALT) and viral load, or the presence of cirrhosis, but investigations for disease assessment are expensive and scarce in resource-limited settings. Here we present a strategy combining two novel point-of-care-tests (POCTs) for (i) quantifying serum ALT (ALT-1) and (ii) IgA2 and dimeric IgA (IgA2/dimer) to determine $\geq$F2 fibrosis, as an inexpensive alternative to laboratory diagnostics.

Methods: Initially, serum from patients with HBV infection in Addis Ababa, Ethiopia, were tested. A derivation cohort comprising 200 selected patient samples were used to determine cutoffs. These were applied to a validation cohort of 105 randomly selected patient samples in the local setting, by local technicians. We then field tested the POCTs at a liver clinic in St Paul's hospital, Addis Ababa with local technicians applying the tests using a droplet of blood on 290 patients with chronic HBV infection.

Results: The ALT-1 POCT applied to serum proved highly correlative with laboratory ALT (AUROC = 0.71); sensitivity to detect ALT >40 U/L was 67-90%. The IgA2/dimer POCT proved effective in identifying patients with $\geq$F2 fibrosis, with sensitivity of 70-82%. In a highly endemic area, the ALT and IgA2/dimer dual-POCT approach identified treatment-eligible HBV patients with 87-88% sensitivity, 32-34% specificity, 42-49% positive predictive value, 75-82% negative predictive value. Among those who had a high viral load, sensitivity was 94-97% for identifying patients meeting EASL criteria for treatment eligibility. Utilisation of fresh blood in a clinical setting only marginally affected test accuracy.

Conclusion: This dual POCT combination is a portable, inexpensive and effective method to immediately identify a majority of those who need treatment for HBV, with potential to be applied at every clinic visit.