EXECUTIVE SUMMARY
(Adapted from the report by SITI MARIAM MOHTAR)

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Background

With an estimated population of 32 million, Malaysia has been reported to have an HCV prevalence of 1.5%, which equates to nearly 330,000 infected adults. The prevalence of HCV infection in haemodialysis was reported to be 3% in haemodialysis patients and 2% in peritoneal dialysis patients in 2016. Due to medical procedures and parenteral exposures, dialysis patients had a higher risk of getting HCV infection compared with general population. Hepatitis C infection in dialysis patients is also associated with poorer survival. The sole use of anti-HCV antibody testing for surveillance of dialysis patients carries the danger that such patients are detected very late and might lead to nosocomial spread of HCV in dialysis unit. Some investigators reported a high rate of false negative serological testing and this justifies the use of nucleic acid testing for detection of HCV RNA among haemodialysis patients. Nevertheless, NAT which include polymerase chain reaction (PCR) method requires considerable high technical skills, costly to perform and entails a robust transport system to ensure sample integrity. Recent development of HCV-core antigen test has the potential to replace PCR as it is less costly. Identifying dialysis patients infected with HCV early is imperative as it will affect the treatment outcomes as well as their quality of life in these patients. This Technology Review was requested by Senior Consultant Nephrologist to review on the evidence of PCR testing versus other testing for HCV detection and the cost-effectiveness of using the tests among dialysis patients.

Objective

To assess the diagnostic accuracy, safety, cost implication as well as organisational aspect of available antibody and antigen screening against nucleic acid testing using PCR in detecting HCV infection in dialysis patients.

Methods

A systematic review was conducted. Review protocol and search strategy was developed by the main author and *Information Specialist*. The following electronic databases were searched through the Ovid interface: Ovid MEDLINE® In-Process & Other Non-Indexed Citations and Ovid MEDLINE® 1946 to 04 August 2020, EBM Reviews – Cochrane Clinical Answers (July 2020), EBM Reviews – Health Technology Assessment (4th Quarter 2016) and EBM Reviews - NHS Economic Evaluation Database (1st Quarter 2016). Parallel searches were run in PubMed, US FDA and INAHTA database. No limits were applied to the search. Additional articles were identified from reviewing the references of retrieved articles. The last search was performed on 30 April 2021.

Results and conclusion:

Diagnostic accuracy/ performance

The results revealed that against PCR, HCV-core antigen showed better performance in terms in sensitivity and specificity compared with anti-HCV antibody and combined HCV-core antigen/anti-HCV antibody tests in detecting HCV infection among dialysis patients. The sensitivity of HCV-core antigen were ranged between 90.7 - 100% and specificity were ranged between 97.4 - 100%. Anti-HCV antibody test showed sensitivity between 31 - 81.8 and specificity of 63.1 - 100%. Combined HCV-core antigen/anti-HCV antibody had sensitivity of 95% and specificity of 94%.

Safety
No safety issues were retrieved regarding the tests.

Organisational issues
A few guidelines suggest two levels of testing. First level of testing being the detection of anti-HCV antibody using either laboratory-based immunoassays or rapid diagnostic test. Following a reactive anti-HCV antibody, WHO (2017) recommended the use the use of quantitative NAT for detection of HCV RNA as the preferred strategy to diagnose viraemic infection. An assay to detect HCV-core antigen, which has comparable clinical sensitivity to NAT, is an alternative to NAT to diagnose viraemic infection based on moderate level of evidence. While MoH CPG (2019) recommended the use of either molecular testing or HCV-core antigen to confirm diagnosis. Patients with on-going risk factors are encouraged to be screened every year which includes patients on long-term haemodialysis.

Economic implication
The results revealed that for screening, PCR alone and combination of anti-HCV antibody test + PCR were the most expensive screening strategy compared with other strategies. Combination of anti-HCV antibody test and PCR was more expensive than combination of anti-HCV antibody test and RIBA as confirmatory test in dialysis patients. One local study showed that replacing Anti-HCV antibody test with HCV-core antigen in screening active HCV infection among haemodialysis patients would not be feasible due to higher cost. However, combining Anti-HCV and HCV-core antigen in detecting HCV infection among haemodialysis patients would generate cost savings.