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Background

Leprosy (also known as Hansen's disease) is an age-old disease affecting mankind with myriad clinicopathological forms. It is a chronic infectious disease caused by *Mycobacterium leprae*. It manifests in various forms based on the immunological profiles and bacterial load in patients. Leprosy is classified as indeterminate, tuberculoid, borderline tuberculoid, borderline, borderline lepromatous and lepromatous leprosy. More recently for therapy purposes, the World Health Organization (WHO) implemented another classification depending on the number of lesions. Patients with five or less skin lesions are considered as paucibacillary cases whereas those with six or more lesions are regarded as multibacillary.

The earliest symptoms are usually skin lesions that are typically flat, pale (hypopigmented) or reddish (erythematous) spots in the skin with slightly decreased sensitivity to touch or pain. These lesions typically do not present with other symptoms, such as burning or pain. There may be some hair loss in the affected area. As the skin lesions progress, they may become raised and, in some cases, nodules may form. The symptoms of nerve involvement include diminished sensation or feeling in the affected areas (anaesthesia) and, sometimes, burning and tingling sensations (paraesthesias). In more advanced cases, there may be weakness, paralysis, and atrophy of muscle in the hands or feet.

According to WHO Weekly Epidemiological Record on global leprosy update in 2020, the registered prevalence of leprosy (the number of cases on treatment at the end of 2020) was 129192, with a rate of 16.6 per million populations. Globally, 127396 new cases were reported for a case detection rate of 16.4 per million populations. Both figures were much lower than in the previous years, with a 27.7% reduction in registered prevalence and a 37.1% reduction in new cases. This change is probably due to less detection and reporting during the COVID-19 pandemic. The highest proportions of both cases registered for treatment (61.1%) and new cases detected (66.6%) were in South-East Asia Region.

In terms of diagnostic, since *Mycobacterium leprae* cannot be cultivated *in vitro*, clinical signs such as presence of lesions, sensory loss and thickened peripheral nerves serve as the primary tool of leprosy diagnosis. However, the disease can easily be confused with other skin pathologies especially by less experienced physicians. Even though the most popular tools like Ziehl-Neelsen and Fite-Faraco staining are available at lower level health institutions of resources-limited countries, their performance in detecting *Mycobacterium leprae* bacilli is low, particularly in paucibacillary patients. Therefore, for these problematic cases, this highlights the need for more sensitive techniques to support clinical diagnosis. Auramine O staining is a fluorescence-based method widely used to detect mycobacterial species such as *Mycobacterium tuberculosis* and *Mycobacterium leprae* and has been previously evaluated to be more sensitive for detection in tissue sections compared to Fite-Faraco and is less time consuming.

Auramine O staining works along with a light emitting diode (LED) fluorescence microscope. A fluorescence microscope is much the same as a conventional light microscope with added features to enhance its capabilities. The conventional microscope uses visible light

(400-700 nanometers) to illuminate and produce a magnified image of a sample. A fluorescence microscope, on the other hand, uses a much higher intensity light source which excites a fluorescent species in a sample of interest. This fluorescent species in turn emits a lower energy light of a longer wavelength that produces the magnified image instead of the original light source.

This technology review was requested by the National Leprosy Control Programme, Disease Control Division, Ministry of Health Malaysia, to evaluate the efficacy, safety, cost-effectiveness and organisational issues related to the LED fluorescence microscope in detecting *Mycobacterium leprae*.

Objective

To evaluate the efficacy, safety, cost-effectiveness and organisational issues related to the light emitting diode fluorescence microscope in detecting *Mycobacterium leprae*.

Methods

Electronic databases were searched through the Ovid interface; Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 1946 to 13 March 2022, Ovid MEDLINE(R) and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations and Daily 1946 to April 7, 2022, Ovid MEDLINE(R) and In-Process, In-Data-Review & Other Non-Indexed Citations 1946 to April 7, 2022, Ovid MEDLINE(R) and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations and Daily 2017 to April 7, 2022, Ovid MEDLINE(R) 1946 to March Week 3 2022, Ovid MEDLINE(R) 1996 to March Week 3 2022, Ovid MEDLINE(R) Epub Ahead of Print April 7, 2022, Ovid MEDLINE(R) Daily Update April 7, 2022 and Ovid MEDLINE(R) 2017 to April Week 2 2022. Searches were also run in PubMed, INAHTA, Cochrane Library and US Food and Drug Administration. Google was used to search for additional web-based materials and information. Additional articles were identified from reviewing the references of retrieved articles. Last search was conducted on 14 April 2022.

Results and conclusion:

A total of 1552 titles were retrieved. After removing duplicates, applying inclusion and exclusion criteria, there were five studies reported on LED fluorescence microscope in detecting *Mycobacterium leprae* included in this review; one case-control study and four diagnostic studies conducted in Ethiopia and India.

Based on the review, the outcomes of the LED fluorescence microscope varied depending on the different skin section taken.

The retrievable evidence showed that, the LED fluorescence microscope works along with Auramine O stain, able to visualise more bacillary load and had higher sensitivity rates compared to Fite-Faraco and Ziehl-Neelsen methods.

There was no retrievable study on the safety of LED fluorescence microscope in detecting *Mycobacterium leprae*. According to the Medical Device Authority Malaysia, there were one fluorescent microscope device (Nova View 2.0 Automated Fluorescent Microscope) and four Auramine O stain registered. The devices had also received 510(k) from United States Food and Drug Administration.

There was no study retrieved on cost-effectiveness of LED fluorescence microscope in detecting *Mycobacterium leprae.* The price range of the technologies depended on types, brands and specifications. Meanwhile, the service charge varied depending on their membership or ward status which was provided by the local provider.