INPLASY PROTOCOL

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Conflicts of interest:
None declared.

A meta-analysis of diagnostic test accuracy of Loop-mediated isothermal amplification (LAMP) test in detection of malaria in pregnancy

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Review question / Objective: **What is the accuracy of LAMP diagnostic test for detection of uncomplicated malaria in pregnancy compared to currently available reference tests?**
Rationale: **To meet the target of malaria elimination, surveillance for submicroscopic infections is crucially important. Strategies to interrupt malaria transmission include prompt identification and treatment of asymptomatic infections. The majority of asymptomatic cases has low parasite densities, undetectable by microscopy or rapid onsite diagnostic test (RDT), but can be identified reliably by polymerase chain reaction (PCR). The use of PCR for case detection could yield higher sensitivity to detect even a single parasite in a blood sample (approximately 10 to 30 µl of blood volume). However, PCR is expensive and requires thermocycling conditions, which is impracticable. Loop-mediated isothermal amplification (LAMP) theoretically enables the detection of low density and sub-microscopic infections with better accuracy and greater ease.**
Condition being studied: **Hence, it is important to utilize a sensitive and accessible diagnostic tool to detect MiP.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 26 March 2021 and was last updated on 26 March 2021 (registration number INPLASY202130096).

INTRODUCTION

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important. Strategies to interrupt malaria transmission include prompt identification and treatment of asymptomatic infections. The majority of asymptomatic cases has low parasite densities, undetectable by microscopy or rapid onsite diagnostic test (RDT), but can be identified reliably by polymerase chain reaction (PCR). The use of PCR for case detection could yield higher sensitivity to detect even a single parasite in a blood sample (approximately 10 to 30 µl of blood volume). However, PCR is expensive and requires thermocycling conditions, which is impracticable. Loop-mediated isothermal amplification (LAMP) theoretically enables the detection of low density and sub-microscopic infections with better accuracy and greater ease.

Condition being studied: Hence, it is important to utilize a sensitive and accessible diagnostic tool to detect MiP.

METHODS

Search strategy: We will use the key terms ("malaria", "diagnosis", "Loop-mediated isothermal amplification"). We will also manually check the references of the relevant reviews for any additional studies.

Participant or population: Pregnant women, regardless of age, parity and locations.

Intervention: Any type of LAMP for diagnosis of malaria.

Comparator: An alternative diagnostic test (e.g. RDT/microscopy).

Study designs to be included: Any study design, if it had evaluated the accuracy of LAMP in detection of malaria.

Eligibility criteria: Studies without sufficient data to construct 2x2 tables were not considered.

Information sources: Health-related electronic databases of PubMed, Ovid, Google Scholar, Cochrane Library, the Latin American and Caribbean Health Sciences Literature (LILACS) and African Journals online (AJOL).

Main outcome(s): Sensitivity, specificity and predictive values.

Data management: Two investigators (LTY and CN) will individually screen the titles and abstracts, and then select the full-text articles according to the inclusion criteria. The two investigators will independently extract the information from each included study using the pre-tested data extraction form prepared for this meta-analysis.

Quality assessment / Risk of bias analysis: The methodological quality of the included studies will be investigated with the use of the revised quality assessment for studies of diagnostic accuracy (QUADAS-2) criteria (Reitsma et a, 2009). It has 3 main domains: Domain 1: patient selection Domain 2: index test(s) Domain 3: reference standard.

Strategy of data synthesis: The data analyses will be carried out through step-wise approach, following the Cochrane Handbook for Systematic Reviews of Diagnostic Test Accuracy (DTA) (Bossuyt et al, 2013), the manual for DTA in STATA (midas) (Jones, 2005; Campbell , 2015). The followings are the steps to apply for data analyses: 1. Creation of diagnostic 2x2 table demonstrating the computation of sensitivity, specificity and predictive values. 2. Summarizing a paired specificity and predictive values for each study in forest plots. 3. Creation of Summary Receiver Operator Characteristic Curves (SROC curves). 4. Calculation of Diagnostic Odds Ratios (DOR) and Area Under the Curve (AUC) to describe test performance across all thresholds. An AUC of 0.5 represents an uninformative test; and an AUC of 1 (where the sROC curve would be in the top left-hand corner in ROC space) represents a test with 100% sensitivity and 100% specificity. 5. Comparing tests using bivariate model This model will estimate the average sensitivity and specificity for each test and the relative sensitivity and relative specificity expressed as odds ratios (ORs) and corresponding 95%confidence interval (CI). 6. Hierarchical summary receiver operating characteristic (HSROC) model. This model is allowing for the reference standard to be possibly

imperfect, and assuming it is conditionally independent from the test under evaluation. 7. Investigation of sources of heterogeneity using meta- regression.

Subgroup analysis: If data permitted, we will make subgroup by i. type of reference test; ii. study countries.

Sensitivity analysis: Sensitivity analysis, based on QUADAS-2 quality domains.

Language: English.

Country(ies) involved: Malaysia.

Keywords: Malaria, Loop-mediated isothermal amplification, Diagnosis, Accuracy, Pregnancy, Meta-analysis.

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