Universal Journal of Public Health 12(5): 892-903, 2024
DOI: 10.13189/ujph.2024.120512

Disparities in the Accuracy of Diagnostics Methods for Arboviral Infection in Africa: A Systematic Review

Running Title: Diagnostic Accuracy for Arboviral Infection in Africa

Abiodun F. Ipadeola[1,*], Timothy A. Attah[2], Olayemi O. Akinnola[1], Olatunji M. Kolawole[3], Grace I. Olasehinde[1]

[1]Department of Biological Science, College of Science and Technology, Covenant University, Nigeria
[2]International Research Center of Excellence, Institute of Human Virology Nigeria, Nigeria
[3]Department of Microbiology/Parasitology, Faculty of Life Sciences, University of Ilorin, Nigeria

Received June 4, 2024; Revised July 31, 2024; Accepted August 23, 2024

Cite This Paper in the Following Citation Styles

(a): *[1] Abiodun F. Ipadeola, Timothy A. Attah, Olayemi O. Akinnola, Olatunji M. Kolawole, Grace I. Olasehinde , "Disparities in the Accuracy of Diagnostics Methods for Arboviral Infection in Africa: A Systematic Review," Universal Journal of Public Health, Vol. 12, No. 5, pp. 892 - 903, 2024. DOI: 10.13189/ujph.2024.120512.*

(b): *Abiodun F. Ipadeola, Timothy A. Attah, Olayemi O. Akinnola, Olatunji M. Kolawole, Grace I. Olasehinde (2024). Disparities in the Accuracy of Diagnostics Methods for Arboviral Infection in Africa: A Systematic Review. Universal Journal of Public Health, 12(5), 892 - 903. DOI: 10.13189/ujph.2024.120512.*

Abstract **Objective:** Laboratory diagnosis for arboviral infection remains a significant public health challenge in Africa. This study reviews the disparities in the accuracy of diagnostic tests for arboviral infection in Africa. **Methods:** A systematic review of studies conducted within the last 10 years was carried out to assess the diagnostic accuracies of arbovirus test methods. Titles were screened for relevance which was followed by screening of abstracts and full texts using the PRISMA guideline. **Results:** A total of 8 full-text articles met the inclusion criteria and were finally selected for the review. 1Step multiplex real-time polymerase chain reaction (RT-PCR), RealStar® yellow fever virus RT-PCR and in-house immunoglobulin M (IgM) capture enzyme-linked immunosorbent assay (ELISA) when compared to their gold standards (RT-PCR and CDC ELISA) showed high sensitivity and specificity in the diagnosis of arboviral infection Majority of the RDTs (RDT SD Bioline Dengue Duo 11FK46, Chembio DPP ® ZCD IgM/IgG and SD Biosensor STANDARD Q Arbo Panel RDTs) also had high diagnostic accuracies with sensitivity and specificity >70%. Luminex technology used in the diagnosis of arboviral infection has also shown high diagnostic accuracy with sensitivity and specificity >80% in the diagnosis of DenV 1,2,3 and 4 nonstructural protein (NS1), and ChikV. However, the diagnostic accuracies for Luminex for DenV 1,2,3 and 4 DIII, and ChikV NS1 were poor. **Conclusion:** The result from this review can be used to stimulate further research and guide policymakers in adopting evidence-based diagnostic techniques to improve diagnosis of arboviruses, case management, and prevention of epidemics.

Keywords Arbovirus, Arboviral Infection, Diagnostic Accuracy, Diagnostic Method, Rapid Diagnosis Test

1. Introduction

Arboviral infections are basically transmitted by arthropods including mosquitoes and ticks and essentially pose a significant impact in Africa. With an incubation period of 2-14 days, arboviral infection can cause various ailments that are frequently displayed with mild febrile illnesses. However, a few cases have been presented with serious and potentially fatal side effects such as encephalitis and haemorrhagic fever [1], [2]. Arboviral infections have also been shown to be transmitted through other means such as blood transfusion, organ transplant,

sexual activity and pregnancy, and birds as well as vertebrates (monkeys, rodents and human) have been identified as reservoirs to this group of viruses [1], [3].

Globally, there are over 250 species of arboviruses of which almost 80 produce human disease and the most commonly recognized are Dengue Virus (DenV), Chikungunya Virus (ChikV), Zika Virus (ZikV), Rift Valley Fever (RVF), and Crimean Congo Hemorrhagic Fever Virus (CCHFV), Yellow Fever Virus (YFV), West Nile Virus (WNV), and Usutu Virus (USUV) [3]. While the frequency and geographic spread of arbovirus outbreaks continue to expand across the globe, there is a need for robust and rapid techniques for prompt and accurate diagnosis, surveillance, and control efforts especially across the African continent and other resources limited regions.

Globally, arboviral infection accounts for about 700,000 related deaths annually [4]. The distribution of arboviral infections is largely dependent on the geographical location as the viruses are predominant in the tropics such as Africa where there are higher densities of these vectors [5]. However, in recent times, cases of certain arboviral infections have been reported in regions not previously seen due to human and environmental factors such as globalization, deforestation and urbanization [6]. Although some of these arboviruses were first identified in Africa, there is little known about the burden of disease on the African population [7], [8], [9]. With 390 million cases occurring annually, DenV is the most predominant arboviral infection and disproportionately affects the Latin American and Asian regions [4], [10]. In Africa alone, the burden of YFV is estimated at about 84,000-170,000 for severe cases and 29,000-60,000 deaths occurring every year [11]. About 160,000 cases and 50 deaths due to ChikV cases were reported globally of which South America was the most affected in March 2024 [12]. Also, an estimated 27,000 cases of ZikV were reported in 2023 [13].

Africa however, is disproportionately affected by arboviral infections due to the occurrence and increase in endemic transmission and periodic outbreaks across the continent [5]. Thus, robust diagnostic capabilities can facilitate prompt identification of these infections and mitigate its impact on the population. The diagnosis of arboviral infections in Africa has evolved significantly in recent years with advances in laboratory techniques, epidemiologic surveillance, and technological innovations. However, poor access to laboratory facilities and healthcare infrastructure, and the presence of co-circulating pathogens with similar clinical manifestations continue to remain a significant challenge [14], [15]. While the diagnosis of arboviral infections in Africa has in time past relied primarily on clinical evaluation, serological assays, and virus isolation techniques, there is a growing need for more rapid, sensitive, and cost-effective diagnostic tools to enhance prompt diagnosis, surveillance and outbreak response efforts [16].

Advancement in molecular biology including polymerase chain reaction (PCR) and next-generation sequencing (NGS) assays has greatly transformed arbovirus diagnostics. However, Point-of-care tests (POCTs) and mobile health (mHealth) platforms are emerging diagnostic technologies for decentralizing timely diagnosis especially in resource-limited settings [16]. It is important that Africa adopts a comprehensive strategy for arbovirus diagnostics that include laboratory-based testing, vector monitoring, epidemiological surveillance, and public health response mechanisms. To improve diagnostic capability and encourage cross-border information exchange and coordination, governments, research institutions, non-governmental organizations, and international agencies must develop collaborative networks and partnerships. This study therefore explores the disparities in diagnostic accuracy of diagnostic tests for arboviral infections in Africa.

2. Method

2.1. Study Design

This study is a systematic review of diagnostic methods for arboviral infections in Africa.

2.2. Key Search Term

The review of articles was performed using Google scholar search engine. Also, relevant references were reviewed for inclusion in the study. The key search terms used for this review were diagnostic strength, diagnostic method, arboviral infection, dengue virus disease, Chikungunya virus disease, Zika virus disease, yellow fever virus disease, West Nile virus disease, rift valley disease, Usutu virus disease, and Crimean Congo virus disease.

2.3. Inclusion and Exclusion Criteria

Only studies that were conducted in the last 10 years (2015-2024), were published in a peer-reviewed journal, and were written or translated into English language were included in this review. Also, articles that had information about sensitivity, specificity, positive predictive value (PPV) and/or negative predictive value (NPV) were included in the review. All other articles that met the inclusion criteria but did not have information about the diagnostic strength were excluded from the review.

2.4. Search Strategy

The literature search was performed in four key stages. In stage one, tittles were screened and those that were relevant to the study were selected. Abstracts of articles with relevant titles were screened based on the inclusion criteria and those with relevant information were selected.

After screening of the abstract, full texts of relevant abstracts that were selected were further screened to meet the inclusion criteria. Only studies that met the inclusion criteria were finally selected into the study.

2.5. Data Extraction

After selection of studies for inclusion into the review, relevant information such as the date and state of study, type of arboviral infection, diagnostic methods, sensitivity, specificity, PPV and NPV were retrieved from the selected studies.

2.6. Quality Assessment

Selected studies were assessed based on the quality of the methodology. This process was performed using the quality assessment tool for diagnostic accuracy studies (QUADAS) [17]. The tool is assessed in four phases and addresses 7 key questions with the risk of bias and applicability assessed for each domain [17]. Overall accuracy scores for all questions were presented in percentages (Supplementary Table 1).

3. Result

3.1. Selection of Studies

Figure 1 represents the literature search output for the systematic review. Out of 9440 Google Scholar outputs, 150 titles were screened with additional 31 references from databases (18) and other sources (13) giving a total of 171 titles. The abstracts of these titles were screened for relevance of which 82 abstracts were excluded from the review. Full texts of the 76 articles were further screened for relevance of which 64 were excluded and only 12 studies were eligible to be included in the review. However, four other studies were excluded due to the lack of data on the sensitivity and specificity and eight studies were finally included in the review.

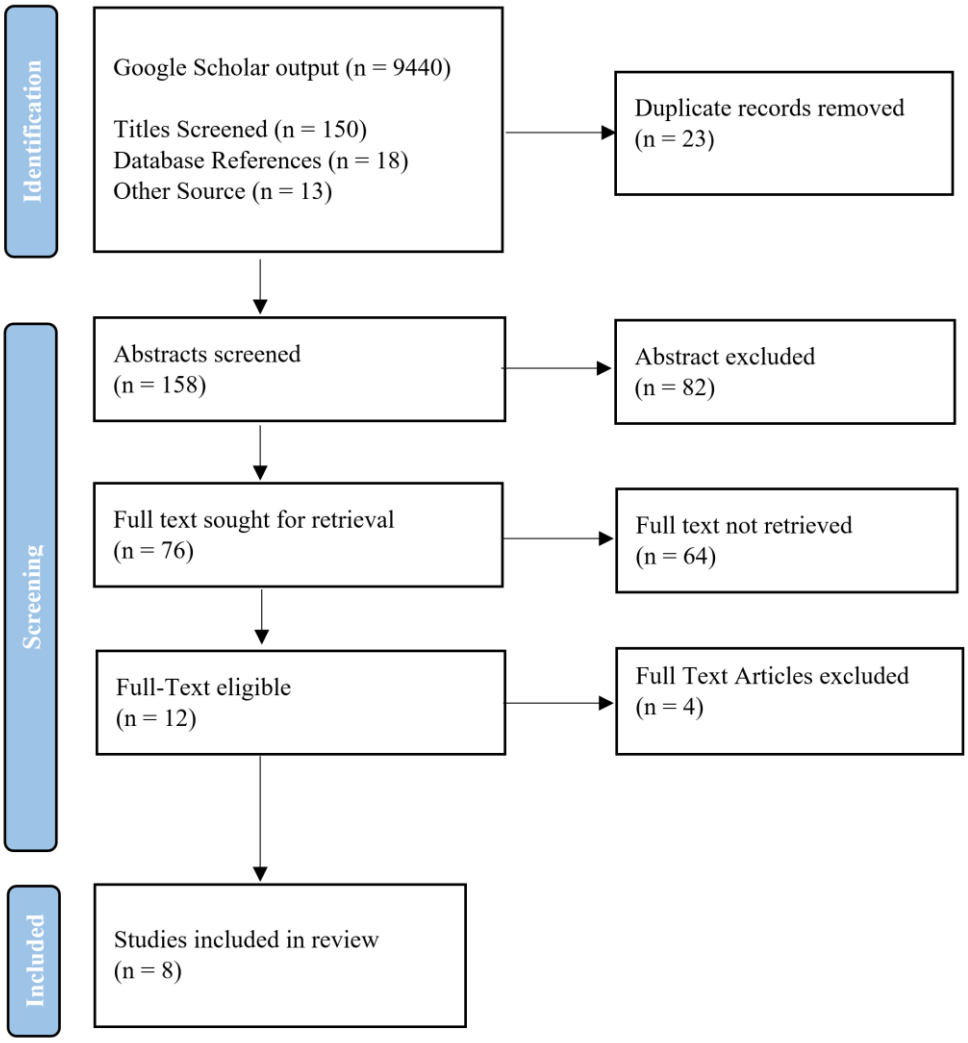

Figure 1. PRISMA Diagram of Search Procedure and Selection of Studies

Using the QUADAS to assess the quality of the study, three studies had scores of >80% while two studies had a total quality score of 72.2%. Two studies had a percentage score of 50-69% while only one study had a total score of 33.3%.

3.2. Study Characteristics

Table 1 represents the number of studies for each arboviral infection diagnostic accuracy tested. Studies included in this review were conducted in Burkina Faso, Senegal, the Democratic Republic of Congo, Cameroon, and Ghana. A total of six arboviral infections were assessed in the studies included in this review. Out of 8 studies included in this review, four each assessed the diagnostic accuracy of DenV and ChikV, while only one study assessed the diagnostic accuracy of WNV and USUV. Three studies assessed the diagnostic accuracy of YFV and two for ZikV. Only one study each assessed the diagnostic accuracy of WNV and USUV.

Table 1. Number of Studies per Arboviral Infections in Africa

Disease	Number of Articles
Dengue Virus Disease	4
Chikungunya Virus Disease	4
Yellow Fever Virus Disease	3
Zika Virus Disease	2
West Nile Virus Disease	1

3.3. Diagnostic Accuracy of Dengue Virus Disease

Table 2 provides the review results for diagnostic accuracy of arbovirus diagnostic methods in articles selected in this review. For DenV diagnosis, two studies assessed the diagnostic accuracy of rapid diagnostic tool (RDT) [18], [19]. One study assessed the diagnostic accuracy of Luminex and real time polymerase chain reaction (mRT-PCR) diagnostic methods in detecting the DenV [20], [21]. One study found that RDT SD Bioline Dengue Duo 11FK46 when compared with PCR as the gold standard had a sensitivity of 90% and a specificity of 99.3% in detecting the presence of non-structural protein (NS1) antigen while the detection of Immunoglobulin M (IgM) antibodies had a sensitivity of 30% and a specificity of 99.3% [18]. The detection of IgG antibody attained 7.6% sensitivity and 99.3 specificity for DenV diagnostic [18]. In another study, the sensitivity and specificity of Chembio DPP ® ZCD IgG test were 90% and 89.2% when compared with enzyme-linked immunosorbent assay (ELISA) [19]. To test for DenV IgM when compared with ELISA, SD Biosensor STANDARD Q Arbo Panel Test had a sensitivity of 71.8% and a specificity of 80.8%[18]. SD Biosensor STANDARD Q Arbo Panel Test also had a sensitivity of 90.0% and a specificity of 90.2% in the diagnosis of DenV NS1 [18]. In one study, when luminiex DenV 1,2,3,4 NS1 was compared to PCR, the sensitivity, specificity, and accuracy of DenV were >80.0% [22]. On the other hand, the sensitivity of Luminex DenV 1,2,3,4 DIII envelope protein in the diagnosis of DenV was <80.0% while the specificity was >90.0% [22]. The diagnostic accuracy of Luminex DenV 1 and 3 DIII was >90.0% while DenV 2 and 4 DIII were <80.0% [22]. In one study, when 1stop mRT-PCR was compared with PCR, the sensitivity and specificity of DenV diagnosis were 90.9% and 100% respectively [21]. Also the sensitivity and specificity of 1stop mRT-PCR when compared with qPCR were 100% [21].

Table 2. Articles Selected for the Review of Diagnostic Accuracy of Testing Tools for Arboviral Infections in Africa

Author, Year, Country	Disease, diagnostic method	Result
Belem et al, 2024, Burkina Faso [21]	DENV, 1Step multiplex quantitative real-time PCR, PCR, Quantitative PCR.	**1stp_mRT_PCR/PCR** Sens: 90.9 Spec:100 **1stp_mRT_PCR/qPCR** Sens:100 Spec:100
Lopez_Jimna et al, 2015, Senegal [23]	CHIKV, RT-LAMP, rRT-PCR	**RT-LAMP/qRT PCR** Sens:100 Spec:80 PPV: 97 NPV:100
Proesman et al, 2015, Congo [18]	DENV, RDT SD Bioline Dengue Duo 11FK46	**RDT SD Bioline Dengue Duo 11FK46/RT PCR NS1 Antigen** Sens:90 Spec: 99.3 **IgM Antibody** Sens:30 Spec:99.3 **IgG Antibody** Sens:7.6 Spec:99.3
Wasonga et al, 2013,Kenya [24]	CHIKV, In-house IgM Capture ELISA, CDC IgM capture ELISA, Focus rduction neutralization test	**In-house IgM Capture ELISA/CDC IgM Capture ELISA** Sens:97.6 Spec:81.3 **In-house IgM Capture ELISA/ FRNT** Sens:91.1 Spec:96.7
Basile et al, 2020, Cameroon [25]	YFV, realstar yellow fever real-time PCR, real-time PCR	**Realstar YFV RT-PCR/RT-PCR** Sens100 Spec:100
Ofosu-Appiah et al, 2021 [20]	YFV , Standard Q yellow fever IgM RDT, real0time PCR	**Q-YF-IgM RDT/RT-PCR** Sens:96.3 Spec:97.94
Raulino et al, 2021 [22]	CHIKV, ZIKV, DENV, USUV, WNV, Luminex assay	**CHIKV** *CHIKV luminex CHIKV E2/PCR* Sens:88.89 Spec: 98.48 Accu:96 *Luminex CHIKV NSP* Sens: 44.4 Spec:98.48 **ZIKV** *Luminex ZIKV DIII/PCR* Spec:96.97 *Luminex ZIKV NS1/PCR* Sens:0 Spec: 98.48 Accu:79

Table 2 continued

		YFV *Luminex YFV NS1/PCR* Sens: 27.78 Spec: 98.48 Accu:83 **DENV** *Luminex DENV1 DIII/PCR* Sens:73.91 Spec:100 Accu:93 *Luminex DENV2 DIII/PCR* Sens:17.39 Spec:98.48 Accu:78 *Luminex DENV3 DIII/PCR* Sens:73.91 Spec:95.45 Accu:90 *Luminex DENV4 DIII/PCR* Sens:26.09 Spec: 96.97 Accu:79 *Luminex DENV NS1/PCR* Sens:91.3 Spec: 98.48 Accu:97 *Luminex DENV2 NS1/PCR* Sens:100 Spec:96.97 Accu:98 *Luminex DENV3 NS1/PCR* Sens:100 Spec:96.97 Accu:98 *Luminex DENV4 NS1/PCR* Sens:82.61 Spec:98.48 Accu:94 **USUV** *Luminex USUV NS1/PCR* Spec:98.48 **WNV** *LuminexWNV NS1/PCR* Sens:100 Spec:96.97 Accu:97 *LuminexWNV DIII/PCR* Sens:100 Spec:98.48 Accu:99

Table 2 continued

Boeras et al, 2021, Africa, Asia, Latin America [19]	ZIKV, DENV, CHIKV,YFV, *Chembio DPP® ZCD IgM test*, *SD Biosensor STANDARD Q Arbo Panel Test*, ELISA	**ZIKA** *Chembio DPP® ZCD IgM test/ELISA* Sens:79 Spec:97.1 *Chembio DPP® ZCD IgG test/ELISA* Sens:92.3 Spec:96.9 *SD Biosensor STANDARD Q Arbo Panel Test/ELISA* Sens:96.8 Spec:90.8 **DENV** *Chembio DPP® ZCD IgM test/ELISA* Sens:90 Spec:89.2 *Chembio DPP® ZCD IgG test/ELISA* Sens:97.5 Spec:96.2 ***DENV IgM*** *SD Biosensor STANDARD Q Arbo Panel Test/ELISA* Sens:71.8 Spec:80.7 ***DENV NS1*** *SD Biosensor STANDARD Q Arbo Panel Test/MAC ELISA* Sens:90 Spec: 90.2 **CHIKV** *Chembio DPP® ZCD IgM test/ELISA* Sens:90.6 Spec:97.2 *Chembio DPP® ZCD IgG test/ELISA* Sens:94.9 Spec:97.2 *SD Biosensor STANDARD Q Arbo Panel Test/ELISA* Sens:84.6 Spec:98.6 **YFV** *SD Biosensor STANDARD Q Arbo Panel Test/ELISA* Sens:86.3 Spec:92

Note: ZikV=Zika virus, DEnV=Dnegue virus, ChikV= Chikungunya virus, YFV= yellow fever virus, WNV= West Nile Virus, USUV= Usutu Virus, Sens= sensitivity, Spec= specificity, PPV= positive predictive value, NPV= negative predictive value

3.4. Diagnostic Accuracy of Chikungunya Virus Disease

Out of the 4 studies that assessed the diagnostic accuracy of ChikV, one study utilized RDT while one each assessed ChikV diagnostic accuracy of RT-LAMP, ELISA, and Luminex. As represented in Table 2, one study included in the review found a good diagnostic accuracy of reverse transcription-loop-mediated isothermal amplification (RT-LAMP) in diagnosing ChikV as the sensitivity and specificity were 100% and 80.0% and the negative predictive value and positive predictive values were 97.0% and 100% respectively [23]. Similarly, another study found that the sensitivity and specificity of Chembio DPP ® ZCD IgM/IgG and SD Biosensor STANDARD Q Arbo Panel Test were >90.0% when compared with ELISA except for SD Biosensor STANDARD Q Arbo Panel Test which had a sensitivity of 84.6% [19]. When In-house IgM capture ELISA was compared with Center for Disease Control (CDC) IgM capture ELISA, the sensitivity and specificity were 97.6% and 81.3% and similar high sensitivity (91.1%) and specificity (96.7%) were found when the same diagnostic method was compared with focus reduction neutralization test (FRNT) [24]. One study found that when Luminex ChikV E2 and NSP proteins were compared with PCR, the sensitivity were 88.9% and 44.4% while the specificity were 98.5% for each diagnostic test [22]. The diagnostic accuracy of Luminex ChikV E2 test method was 96.0% [22].

3.5. Diagnostic Accuracy of Yellow Fever Virus Disease

As presented in Table 2, two out of the three studies assessed the diagnostic accuracy of RDT compared to PCR/ELISA while one assessed the diagnostic accuracy of realstar YFV RT-PCR. In these two studies, the sensitivity and specificity of Q-YF-IgM RDT and SD Biosensor STANDARD Q Arbo Panel Test when compared with PCR and ELISA were >90.0% except for SD Biosensor STANDARD Q Arbo Panel Test which had a sensitivity of 86.3% [19], [20]**.** The other study that assessed the diagnostic accuracy of realstar YFV RT-PCR compared with RT-PCR found that the sensitivity and specificity in the diagnosis of YFV were 100% each.

3.6. Diagnostic Accuracy of Other Arboviral Infections

Out of the two studies that assessed the diagnostic accuracy for ZikV, one study found that the specificity of Luminex ZikV DIII and ZikV NS1 proteins when compared with PCR were 96.9% and 98.5% while the sensitivity were poor [22]. Diagnostic accuracy for Luminex ZikV NS1 protein was 79.0% [20]. Another study found that the sensitivity and specificity of Chembio DPP ® ZCD IgM, Chembio DPP ® ZCD IgG, and SD Biosensor STANDARD Q Arbo Panel Test RDTs in diagnosing ZikV when compared with ELISA were >90.0% except for Chembio DPP ® ZCD IgM and IgG which had sensitivity of 79.0% [19], [25]. For the diagnosis of WNV, one study found that Luminex WNV NS1 and Luminex WNV DIII had sensitivity and specificity >90.0% when compared to PCR [22]. Luminex USUV NS1 when compared with PCR had a specificity of 98.5% in the diagnosis of USUV [21].

4. Discussion

In this study, we reviewed the literature related to arboviral infection diagnosis in Africa to understand the diagnostic accuracy in terms of sensitivity, specificity, PPV, and NPV. Generally, studies included in this review assessed the diagnostic accuracies of PCR, ELISA, multiplex Luminex, and RDT tools for 6 arboviral infections (DenV, ChikV, ZikV, YFV, WNV, and USUV) in Africa. However, only one study assessed the PPV and NPV of diagnostic tools while all other studies assessed the sensitivity and specificity respectively.

In our review, one study found that 1Step mRT-PCR when compared with conventional PCR and qPCR had sensitivity and specificity of >90.0% [21]. This is consistent with a finding from a study conducted on Nicaraguan samples where the sensitivity in the detection of DenV was 100% and specificity 97.2% [26]. The RealStar® Yellow Fever Virus RT-PCR Kit is a diagnostic assay developed by Altona Diagnostics for the detection of YFV ribonucleic acid (RNA) in clinical specimens using RT-PCR technology [27]. RealStar® YFV RT-PCR Kit represents a valuable tool for the molecular diagnosis of YFV and has been found to have high sensitivity and specificity in the rapid detection of YFV RNA in clinical specimens [27]. In our review, a similar finding was identified as one study reported 100% sensitivity and specificity of realstar YFV RT-PCR in detecting YFV in blood samples [25]. Thus, this diagnostic has the potential for prompt diagnosis with early turnaround time making it a valuable tool for surveillance and response to YFV in endemic regions.

One study reported sensitivity and specificity of >80.0% for in-house IgM capture ELISA when compared with CDC IgM capture ELISA and FRNT [24]. Although the study in our review assessed the diagnostic accuracy in detecting DenV IgM, other studies have reported an in-house ELISA-based test to have sensitivity and specificity of >70.0% in the diagnosis of IgG antibodies for ChikV [28], [29], [30]. Previous studies have detailed how ELISA can be used for the rapid diagnosis of specific arboviral infections that are medically important [31], [32], [33]. These individual ELISA procedures likely involve the detection of antibodies or antigens specific to a particular arbovirus in patient samples. Some of these individual ELISA procedures have been modified and combined to create comprehensive assay sets. These sets are designed to detect IgM antibodies, which is produced early in the course of an acute infection. In MAC-ELISA, antigens

specific to the arbovirus are immobilized on the ELISA plate, and IgM antibodies present in samples are captured by these antigens [34]. Although ELISA-based test is a generally accurate, reliable, and versatile technique used to detect the presence of arboviral infection, this technique often requires specialized laboratory equipment, skilled personnel, adequate storage and transport, and is relatively expensive to purchase and maintain and this can be challenging in resource-limited settings.

A study included in this review found that RDT SD Bioline Dengue Duo 11FK46 compared to PCR had a sensitivity and specificity >90.0% in diagnosing DenV NS1 protein while the sensitivity of IgG and IgM antibody were poor [18]. This is similar to a study on clinical samples in Colombia which found sensitivity and specificity of >70.0% in the diagnosis of DenV [35]. However, other studies conducted in Brazil and France found that SD BIOLINE Dengue Duo RDT had <50.0% sensitivity in the diagnosis of DenV NS1 which is contrary to our finding in one of the studies included in this review [35], [36]. A similar poor sensitivity of DenV IgM was reported in another study [35]. Our review found that Chembio DPP ® ZCD IgM/IgG and SD Biosensor STANDARD Q Arbo Panel RDTs used in the diagnosis of ChikV when compared to ELISA had sensitivity and specificity >80.0% [19]. However, another study conducted in Thailand reported poor sensitivity and specificity of Chembio DPP ® ZCD IgM/IgG in the diagnosis of ChikV antibodies. This may be due to differences in geographical locations, strain of the virus, or variation in storage and handling of test kits. Chembio DPP ® ZCD IgM/IgG, and SD Biosensor STANDARD Q Arbo Panel tests when compared with ELISA had sensitivity and specificity >70.0% in the diagnosis of ZikV [19], [22]. Other RDTs have equally shown high diagnostic accuracy with Chembio DPP ® ZCD IgM and IgG test/ELISA, and Q-YF-IgM RDT/RT-PCR having sensitivity and specificity >80% [19], [20].

There are several advantages that RDTs offer over traditional laboratory-based techniques like ELISA and PCR, particularly in resource-limited areas. These include the ease of use, point of care testing, rapid results, relatively low cost, multiplexing capabilities and importance in surveillance and response. However, it is important to take into consideration its limitations as some RDTs have much lower sensitivity and specificity compared to other laboratory tests. Thus, identifying the most accurate and reliable RDTs is necessary to promote prompt diagnosis and treatment of arboviral infections.

One study in our review found sensitivity and specificity of >80.0% of Luminex in the diagnosis of DenV 1,2,3 and 4 NS1 protein while the sensitivity of DenV 1,2,3 and 4 DIII was <80.0% [22]. Multiplex microsphere assays have also been used in the diagnosis of IgG or IgM for other arboviral infections [25]. However, diagnostic accuracy may vary based on geographical location, duration of onset of clinical features, or the isotope of the antibody [37]. One study in our review found that Luminex ChikV E2 had sensitivity and specificity >80.0% when compared to PCR in the diagnosis of ChikV while Luminex CHIKV NS1 had a poor sensitivity [22]. Other studies have also identified this multiplex tool as a vital diagnostic tool for the identification of mosquito-borne pathogens and surveillance and response purposes [38]. This technology can simultaneously detect multiple targets (antigen and antibodies) in a single assay thus, making the method useful in identifying ChikV as well as other arboviral infection antigens and antibodies or co-infection in infected samples [38]. As identified in a study included in this review, Luminex assay has high sensitivity and specificity allowing for the accurate and reliable detection of ChikV, and only requires a small patient sample volume. Luminex tool has also been found to show high sensitivity and specificity in the diagnosis of WNV and USUV [22]. This makes it a valuable diagnostic method for surveillance and research purposes and is a suitable diagnostic tool for resource-limited regions. However, a study in this review found that although luminex had high specificity and accuracy, the diagnostic tool had poor sensitivity in detecting ZikV NS1 protein [22].

5. Summary

In this review, 1stp_mRT_PCR, RDT SD Bioline Dengue Duo 11FK46 (NS1 Antigen), SD Biosensor STANDARD Q Arbo Panel Test (DenV NS1), Chembio DPP ® ZCD IgM test had high sensitivity and specificity (>80%) when compared to the PCR or ELISA while either sensitivity/specificity of RDT SD Bioline Dengue Duo 11FK46 (IgM and IgG antibodies), luminex (DenV1,2,3 and 4 DIII) SD Biosensor STANDARD Q Arbo Panel Test (DenV IgM) were low (<80%). Studies in our review also found that all test for ChikV had relatively high diagnostic sensitivity and specificity when compared with PCR or ELISA. For YFV, all diagnostic tests in this review were found to have high sensitivity and specificity (>80%). Apart from chembio DPP ® ZCD IgM test, all other diagnostic test reviewed in this study had high sensitivity and specificity in the diagnosis of ZikV. Lastly, the sensitivity and specificity of Luminex USUV NS1and WNV DIII when compared to PCR were high in the diagnosis of USUV and WNV.

6. Study Limitations and Strength

Our review has some limitations. Except for one study, only two of the four key indicators were assessed in studies included in this review which affected the possibility of providing a review as to the comprehensive assessment of diagnostic accuracies of diagnostic tools utilized taking into consideration both the ability to correctly identify true cases of arboviral infections and the potential of

misdiagnosis. Also, only 8 studies met the inclusion criteria and were included in the review revealing the great dearth of scientific knowledge about the diagnosis of arboviral infections in Africa where these infections are predominant.

Recommendation

With evidence from studies included in this review, we found that while other advanced diagnostic tools may be relatively expensive and inaccessible to resource-limited countries like in Africa, RDTs and Luminex diagnostic tools have shown good diagnostic accuracies in the diagnosis of arboviral infection. Therefore, we recommend that countries adopt the use of these diagnostic tools in the integrated diagnosis and surveillance of arboviral infections. Also, there is a need for other studies to improve scientific knowledge about the diagnostic accuracies of the available diagnostic tools in detecting the presence of the wide range of arboviral infections that are distinct to the African region. Studies should also aim towards assessing the PPV and NPV of diagnostic tools in detecting the presence of these arboviruses in order to provide adequate data on the diagnostic accuracies of diagnostic tests.

Appendix

Appendix 1. Quality Assessment of Studies included in the Review

		R1	R2	R3	R4	R5	R6	R7	R8
Patient Selection	**Risk of Bias**								
	Was a consecutive or random sample of patient enrolled	1	0	1	1	0	1	0	1
	Was a case-control design avoided?	1	1	1	1	0	1	1	1
	Did the study avoid inappropriate exclusion	1	1	1	1	0	1	0	1
	Could the selection of patients have introduced bias	0	0	1	1	0	1	0	1
	Applicability								
	Is there concern that the included patients do not match the review question	1	1	1	1	0	1	1	1
Index Test	**Risk of Bias**								
	Were the index test results interpreted without knowledge of the results of the reference standard	1	0	1	0	0	1	0	0
	If a threshold was used, was it pre- specified	1	1	1	0	1	1	0	1
	Could the conduct or interpretation of the index test have introduced bias	1	1	1	0	0	1	1	1
	Applicability								
	Is there concern that the index test, its conduct or interpretation differ from the review question	1	1	1	1	1	1	1	1
Reference Standard	**Risk of Bias**								
	Is the reference standard likely to correctly classify the target condition	1	1	1	1	1	1	1	1
	Were the reference standard results interpreted without knowledge of the results of the index test	1	1	1	0	1	0	0	0
	Could the reference standard, its conduct, or its interpretation have introduced bias?	1	1	1	1	1	1	1	1
	Applicability								
	Is there concern that the target condition as defined by the reference standard does not match the review question?	1	1	1	0	1	1	1	1
Flow and Timing	**Risk of Bias**								
	Was there an appropriate interval between index test(s) and reference standard?	0	0	0	0	0	0	0	0
	Did all patients receive a reference standard?	1	1	1	0	0	1	1	1
	Did patients receive the same reference standard?	1	1	1	1	0	1	1	0
	Were all patients included in the analysis?	0	0	0	0	0	0	1	0
	Could the patient flow have introduced bias?	1	1	1	0	0	1	1	1
	Score	**15**	**13**	**16**	**9**	**6**	**15**	**11**	**13**
	Percentage	**83.3**	**72.2**	**88.9**	**50.0**	**33.3**	**83.3**	**61.1**	**72.2**

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