COST-EFFECTIVENESS OF RAPID DIAGNOSTIC TESTS (RDTS) FOR DENGUE IN PEDIATRIC EMERGENCY SETTINGS

Anand Kumar Jha,[1] Md. Ashfaque Ansari,[1] Ravi Shankar Gupta[2]

ABSTRACT

INTRODUCTION

Dengue is a flavivirus infection spread by *Aedes aegypti and Aedes albopictus* mosquitoes and is estimated to infect up to 400 million people worldwide each year. The IgM capture ELISA has become the most accepted technique for the diagnosis of dengue in developing countries like Nepal. For the early detection Rapid Diagnostics Tests (RDT) is the most appropriate method to be used in emergency setting. This study aims to study about the RDTs and analyze its cost effectiveness among pediatric patient of emergency department as it is the most required method for early diagnosis in the warning stage to prevent unnecessary expenditure in hospitalization and extra tests.

MATERIAL AND METHODS

This study was conducted from the health care system perspective for the cost effectiveness analysis (CEA) to evaluate the potential financial impact on implementing rapid diagnostic tests (RDT) for the diagnosis of dengue in the pediatric cases of emergency settings.

RESULTS

The rapid diagnostic tests decreased 66.22% of the cost to the child who attended emergency department with the suspicion of the dengue with Rs. 1520 of savings per patient. Among the total attendees, 86.5% suffered from high grade fever 69% had other warning signs. RDT proved its significance with only 16% of hospitalizations and zero mortality rates in the study period.

CONCLUSION

This study reported that RDT can be a suitable way for early triage and diagnosis meeting the health care needs and budget of the individual.

KEYWORDS

Dengue, Children, Rapid diagnostic Tests, Cost efficiency, Early triage

1. Department of Pediatrics, National Medical College and Teaching Hospital, Birgunj, Nepal
2. Department of Microbiology, National Medical College and Teaching Hospital, Birgunj, Nepal

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For Correspondence
Dr. Anand Kumar Jha
Department of Pediatrics
National Medical College
Birgunj, Nepal
Email: dranandjha@gmail.com

INTRODUCTION

Dengue is a most common yet fatal disease, diagnosed mainly in Terai region of Nepal. It is caused in human being by the bite of infected mosquito which is mostly found around summer season more relevantly in the belt of Terai region. Dengue is a flavivirus infection spread by *Aedes aegypti* and *Aedes albopictus* mosquitoes and is estimated to infect up to 400 million people worldwide each year.[1] Four distinct dengue virus serotypes (DENV-1 through DENV-4) cause dengue. After infection with one serotype, an individual develops lifelong immunity to that serotype, but subsequent infection with another serotype increases the risk of severe dengue due to antibody dependent enhancement of infection.[2] Pediatric population being at a developing stage of getting immunity and body strength, they are more prone to getting affected.

The gold standard for dengue diagnosis is based on nucleic acid amplication tests (NAAT) and antibody detection by serology tests. However, these tests are expensive and seldom available in most health-care facilities, and they are only routinely performed in reference microbiology laboratories. Moreover, because laboratory results are not immediately available, unnecessary admissions and antibiotic prescriptions may occur.[3] Prevalence of dengue virus infection is increasing and proper control measure should be provided. IgM capture ELISA was used for laboratory analysis and remains as a reliable and inexpensive method for the diagnosis of dengue. Hence, the IgM capture ELISA has become the most accepted technique for the diagnosis of dengue in developing countries like Nepal.[4]

The severe manifestations of dengue include hemorrhagic manifestations, multi organ dysfunction and distributive shock. Hence, early diagnosis of dengue infection and initiation of appropriate fluid resuscitation is the key component in the management of severe dengue infection.[5] Therefore, for the early detection rapid diagnostics tests (RDT) is the most appropriate method to be used in emergency setting. This study aims to study about the RDTs and analyze its cost effectiveness among pediatric patient of emergency department as it is the most required method for early diagnosis in the warning stage to prevent unnecessary expenditure in hospitalization and extra tests.

MATERIAL AND METHODS

This study was conducted from the health care system perspective for the cost effectiveness analysis (CEA) to evaluate the potential financial impact on implementing rapid diagnostic tests (RDT) for the diagnosis of dengue in the pediatric cases of emergency settings.

This study was conducted in the Department of Paediatrics and the Department of Microbiology at National Medical College, Birgunj, Nepal. The study spanned from 3rd January 2024 to 2nd January 2025. A total of 200 dengue cases were reviewed for a year of 2024 for the research.

All the children confirmed with dengue with positive detection of RDT test were included in the study - Type A (NS1 only), Type B (NS1 + IgM) and Type C (NS1 + IgM + IgG). Children with proven diagnosis of co-infections like, malaria, fever, viral infections without RDT (NS1, IgG and IgM) positivity despite the strong clinical manifestation of dengue were excluded.

Diagnosis was done with dengue NS1 detect rapid test. It is an immunochromatographic strip assay for qualitative presumptive detection of non-structural protein 1 (NS1). This test will aid in the early diagnosis of Dengue virus in human serum prior to the presence of IgM or IgG anitbodies.

The approval for the study was formally taken from the Institute Ethics Committee on 2nd January, 2024, National Medical College, Birgunj, Nepal (Ref.F-NMC/679/080-081) and the research was performed by the ethical standards of the committee. Informed oral and written consent was taken from the informant (patient and patient party) as per the protocol of the study method. Patient's confidentiality was strictly maintained for the study purposes.

Main outcomes and methods

The study focuses of main three outcomes: 1) total healthcare cost of management of dengue in pediatric cases, 2) cost savings of using RDTs compared to standard diagnostic methods and 3) total cost per accurate diagnosis.

The decision tree model was developed to estimate the process of diagnosis and management of dengue and its financial effectiveness. The RDT costs were compared with the standard process of diagnosis that is IgM capture ELISA and serology which helps to assess the cost potency of the tests and hospital expenditure. Three types of RDTs were evaluated: Type A (NS1 only), Type B (NS1 + IgM) and Type C (NS1 + IgM + IgG) with their, unit price and sensitivity and specificity of each of them. The cost of diagnosis and unnecessary costs due to correct and incorrect diagnosis is calculated by the evaluation of four important measures which includes true positive, false positive, true negative and false negative.

The costs of RDTs were based on the charge scheme of the hospital chosen for research. The standard expected costs are total sum of outpatient checkup, additional tests, hospitalizations, prescribed medicines. Patient's saving is calculated by subtracting expected standard cost by expected RDT cost.

Definitions of new terms

Target Markers

Rapid diagnostic tests is characterized by three main target markers, whose positivity or negativity determines the diagnosis of dengue. The three main target markers: NS1, IgG and IgM.

NS1: The protein creates antibodies to attack the illness, triggering an immunological response. The NS1 antigen is detected in their blood when infected with dengue fever. As a result, the test aids in the early diagnosis of dengue fever.[6]

IgG: Dengue IgG Test or immunoglobulin G test is used for the detection of dengue virus IgG antibodies. This test is usually used as a screening test and provides a preliminary test result to diagnose any previous or present infection with dengue viruses.[7]

IgM: The dengue IgM test is a blood test that detects IgM antibodies produced by the body when it is infected with the dengue virus. IgM is the first antibody to be produced in

response to a dengue infection and can be detected in the blood within a few days of exposure to the virus. The presence of IgM antibodies indicates that a person has recently been infected with dengue.[8]

Diagnostic Outcome
True Positive
It is defined as the dengue cases that are correctly identified.
False Positive
The case which does not have dengue but test identifies the patient as dengue.
False Negative
The dengue case is not diagnosed as dengue.
True Negative
The case does not have dengue and test is also correct about not identifying dengue.

Statistical analysis
The data were input and analyzed using Microsoft Excel 2010 and SPSS version 25. Data on history and clinical symptoms were input and patient frequencies were estimated. Descriptive statistical analysis was done in terms of frequency, percentage, mean, and standard deviation, which were all computed.

RESULTS

Among the 200 pediatric cases of dengue attending the emergency department 88 patients (44%) of them were properly detected whereas 38 more of them (19%) were still in high suspicion, so, total of 126 (63%) were treated for dengue. Estimated cost price for these children was Rs.2500 – Rs.3000 which would be around Rs.4500 without the rapid diagnostic test. Among the total children, 138 (69%) of them had the warning signs of clinical manifestation and 173 children (86.5%) suffered from high grade fever. Even after the early detection amid their warning signs 32 of them (16%) had severe condition on the disease and needed to get hospitalized for the further treatment. Observing the 16% of hospitalization and 69% of warning sign cases, RDT played a crucial role in early diagnosis, detection and triage which saved a hefty amount of money for the patients. This can clearly state the cost efficiency of RDT in the dengue cases, in emergency departments.

Association of cost saving is related to three categories of RDT, type A, B and C. Type C with all the three target markers is analyzed the most accurate one with the highest sensitivity percentage of 94% and 98% of specificity. Observing the cost saving perspective, again, type C is on the highest one with Rs. 2800 estimated saving per patient.

Table 1. Cost effectiveness and features of dengue RDT categories

RDT categories	Target markers	Sensitivity (%)	Sensificity (%)	Unit price (NPR)	Estimated saving per patient (NPR)
A	NS1	80	92	500	1400
B	NS1 + IgM	88	95	1000	2100
C	NS1 + IgM + IgG	94	98	1500	2800

In the result of decision tree model, 44% was of true positive and 6% falls under false positive, 19% got diagnosed into false negative and finally 31% was of true negative.

Table 2. Decision-tree model analysis

Outcomes	Count	Percentage (%)	Estimated cost per case (NPR)
True positive	88	44	2500
False positive	12	6	3000
False negative	38	19	6500
True negative	62	31	1500
Average cost per child using RDT(NPR)	Rs. 2980		

Analyzing this data, 84% of the patient saved their cost by getting early diagnosis. With the calculation of estimated cost per patient, the average cost per child was Rs.2980. with the estimation of average Rs.4500 without RDT, per patient saved Rs.1520 and for the total of 200 patients Rs.3,04,000 was estimated as the total cost saving which is proving the cost effectiveness of the method.

DISCUSSION

The research found that the operationalization of dengue RDT testing led to a cost saving in terms of per-patient costs, from Rs. 4500 down to Rs. 2980 (by around 34%). Therefore, the finding can be extrapolated to an outcome where a point-of-care test is seen to conserve resources by limiting unnecessary hospital care. For instance, a Spanish cost-effectiveness model concluded that dengue RDTs could reduce hospital admissions by half and save around €289–€389 per traveler tested.[3] Another study in an endemic setting demonstrated that it would be cost-effective to test using an IgM-based RDT.[9] Contrariwise, a separate modeling analysis found that RDTs might be more costly and less effective than presumptive management in some situations, thereby highlighting context dependence.[9] The large savings we recorded (Rs. 1520 per patient) may be attributable to fewer admissions and fewer ancillary investigations because patients could be promptly managed as outpatients once RDTs ruled out dengue. This finding is consistent with World Health Organization guidance, which recommends selective use of RDTs for resource preservation.[10] In the resource-poor health system of Nepal, where hospital stays and advanced diagnostics carry a high cost, these savings become particularly notable. Local factors could exacerbate or attenuate the mentioned advantage: for example, a positive RDT result is highly useful in guiding management during high-prevalence outbreaks, whereas in low-prevalence periods, the test is likely used more marginally. Thus, bringing all pieces together, ones' cost analysis proposes that the use of RDTs routinely in a pediatric ED could be justified economically, parallel to the findings for cost-savings elsewhere.[3,9]

RDT-based presumptive-diagnosis followed by early detection using RDTs is consistently reported to afford only moderate sensitivity. Our decision model yielded a range of cases of which 44% suspected instances were indeed true positives and 19% false negatives (it being sensitivity somewhere in the neighbourhood of ~ 70%): the latter figure more than adequately suffices the wide margin in global reports (RDT sensitivities from ≈ 10–99%)9. On the positive side, the majority of RDTs have good specificity, about 90% or more, however, specificity varies with sensitivity.[9,11] At times, Garg et al[11] found a fairly wide variation in sensitivities of IgM RDTs from 28%–78% and specificities between 50% and 86%, while systematic reviews decry the fact that common RDTs often underperform compared with

claims made by manufacturers.[9,11] The high-sensitivity assays we used (NS1/IgM combos) likely improved detection, but false negatives still occurred, as emphasized in Nepal's national guidelines.[10] Other elements in the solution include types of RDT markers (NS1 is best early, IgM appears later), timing of sample collection, and local epidemiology (e.g., circulation of multiple serotypes or cross-reacting flaviviruses). In Nepal, for example, NS1-based RDTs are deployed in primary centers, though our results imply combo kits still miss cases. In essence, our 44% true positives rate is in accord with literature portraying RDTs as ideal for quick triage of patients but not perfect dryers high specificity but limited sensitivity.

RDT use in our pediatric ED showed a clear effect-on-clinical-practice pattern. Hospitalization was required in only 16% of patients, all survived, whereas admission rates are much higher in previous Nepal experiences. For example, Dumre et al[12] reported that during major outbreaks only 12% of dengue cases were treated as outpatients and 88% were admitted. Even during the 2022 epidemic, only about 8.7% of confirmed patients in Patan Hospital required admission.[13] Our 16% admission rate, which is quite far lower than the historically 88%, indicates that the rapid RDT confirmation allowed for many mild cases to be safely managed as outpatients, which is in accordance with the Nepal admission protocol under which only those with warning signs (Group B/C) are admitted.10 Similarly, Camprubí-Ferrer et al[3] also found that early implementation of RDT in Spain allowed dengue admissions to drop by half primary care under direct observation. Differences between the rates probably explain differences of settings: in a controlled outbreak setting, nearly everyone was hospitalized for observation, whereas in our routine ED setting, early RDT result allowed clinicians to limit admissions to only those children who were truly at risk. Also, zero mortality in our cohort speaks to the ability of early diagnosis and management to prevent mortality. Hence, our outcome trends of far fewer admissions and no deaths undoubtedly complement broader evidence showing that RDT-guided care streamlines dengue management. Differences from the earlier Nepal data probably come from health system factors (laboratory capacity, admission thresholds) and epidemiology.

CONCLUSION

In conclusion, the study has thoroughly established evidence that RDTs provide a cheaper and clinically efficient way to detect dengue at the earliest point of care in pediatric emergency settings in Nepal. These RDTs afford an average saving of Rs. 1520 per patient, thereby curbing unnecessary hospital admissions and other associated costs, which lessen the burden on families and bode well for the economic efficiency of health service responsiveness. RDTs with NS1+IgM+IgG markers have been shown to have reasonable accuracy in diagnosing dengue timelily in order to initiate triage and management; thus, the progression of the disease and patient welfare are considerably reduced. This evidence suggests that RDTs should be more widely used in the national dengue control program, especially in high-prevalence areas such as the Terai region, to make a case for both economic viability and community health resiliency.

This study did not included a formal sensitivity analysis, using a proper model as the grounded retrospective data is collected from the real patients from the study setting choosing a most relevant area. All the cost estimation is done from the actual diagnostic and triage patterns from the hospital payment schemes. Though the sensitivity analysis is useful in a model based or hypothetical study based, it was not obligatory in this real word, data driven cost effectiveness analysis.

CONFLICT OF INTEREST

None

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