Analysis of Total Number of Dengue Screening Test sent using Standard Versus Modified Protocol

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ABSTRACT

Introduction: Patan Academy of Health Sciences (PAHS) emergency department adopted a standard protocol for case management which was further modified to sustain the influx of patient. In standard protocol dengue test was sent for all patient while in modified protocol the test was sent in limited patients. This study was designed to predict the number of investigations that would have been sent using these protocol during the outbreak.

Methods: This was a cross sectional study conducted at emergency department of PAHS, during a dengue outbreak (September 2019). Patients with a screening test sent and those with a positive screening test were analyzed using regression for the number of dengue screening test sent using standard and modified protocol.

Results: Total of 10,773 patients visited emergency department from 15 August to 14 October 2019. Suspected dengue was 2567 (23.8%), out of which dengue screening test was positive in 658 patients. Standard protocol was used in phase 1, the median test sent per day was 95.5, if modified protocol had been used the median test would have been 89.0, this was statistically significant. In phase 2 median test sent per day using modified protocol was 60.5, if standard protocol had been continued median test would have been 61.0 per day. It was not statistically significant.

Conclusions: Modifying protocol according to surge of patient during epidemic is helpful if it is sent early during outbreak. Case management protocols need to be dynamic to manage the surge of patient.

Keywords: dengue; disease outbreaks; surge capacity.

INTRODUCTION

The World Health Organization (WHO) released dengue management guideline in 1997[1] which was further revised in 2009 and additional document to manage dengue were released in 2011 and 2012.[2] The revised national guidelines on dengue prevention, management and control, 2019 has claimed to provide a technical 'gold-standard' advice on all aspects of dengue.[3]

In September 2019, Nepal faced dengue outbreak[4], the rising number of cases were managed in different hospitals and emergencies.

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Emergency department of Patan Hospital also observed dengue patients exceeding the human resources and diagnostic kits. So, the standard protocol was modified to manage this influx of patient. This study is designed to predict the number of investigations that would have been sent if modified protocol[5] or standard protocol had been used throughout the outbreak month. This will help to implement the suitable protocol as soon as outbreak is established in future.

METHODS

This was a cross sectional study aimed to review the records of number of patients visiting emergency department of Patan Academy of Health Sciences, Patan Hospital during outbreak of dengue (September 2019). The objective of this study was to analyze the prediction module in time series for the number of dengue screening

test sent using standard and modified protocol.

Records of all patients presented to emergency as suspected dengue was be retrieved from the record section of Patan Hospital. During outbreak, as a routine procedure, the record section of Patan Hospital collected detail of all suspected dengue patients. The record consisted of the following parameters in excel sheet: serial number, date, name, age, gender; NS1 antigen, IgG and IgM positive or negative status. Total number of patient presenting to emergency during that period (September 2019) was also be retrieved from the record section. To analyze the trend, the total patient visiting a month before (August 2019) and a month after (October 2019) outbreak was also analyzed.

All patient with suspected dengue was included in the study. Incomplete demographic (missing age, sex) records and inconclusive lab diagnosis (NS1 antigen, IgG or IgM antibody – weak positive) was exclusion criteria. Since this study included only patient whose lab investigations has been send, those patients whose lab investigations were not sent were excluded automatically.

Suspected Dengue (Test sent) was defined as patient presenting with fever during this epidemic period whose screening test had been sent; highly suggestive (Screening test positive) was defined as patient whose NS1 antigen, IgG or IgM for dengue was positive.[3] These were available rapid diagnostic test (RDT) at Patan Academy of Health Sciences during outbreak. These are screening tests, and does not confirm diagnosis. Diagnostic tests were not available at Patan Hospital. All patient visiting emergency of Patan hospital during that period were labelled as 'Total Patient'. Guideline published by epidemiology and disease control division, Government of Nepal[3] was considered as standard guideline. The warning signs, clinical examination and investigation (NS1 antigen, IgG and IgM antibody, total count, platelet and hematocrite) for the diagnosis and treatment mentioned in the guideline published by Government of Nepal was included in the standard guideline. The guideline which was

modified by department of general practice and emergency medicine, Patan Academy of Health Sciences (PAHS) during dengue outbreak to manage the increasing influx of the patient was considered as modified guideline.[5] This guideline focuses more on warning signs and clinical examination (abnormal vitals, seizure, dizziness, drowsiness, headache not relieved by initial dose of paracetamol, shortness of breath, severe chest or abdomen pain, any localized clinical or neurological findings, decrease urine output, bleeding from any sites) and investigation was sent only for patients having warning signs. Rapid diagnostic test (RDT) done via kit and was considered as screening test. [3] This will include NS1 antigen, IgG and IgM antibody test. The screening kit was supplied by Biotrol Laboratories Pvt. Ltd, New Delhi-110015.

The modified guideline was developed based on available guideline and protocols[1-3] so construct validity was achieved. Content and face validity were achieved by consensus of the department. Criterion validity and reliability of the tool was not tested.

The timeline that was used for the analysis of data were as follows:

1. August 30, 2019 (Phase 1): Patan academy of health sciences started getting dengue positive cases from last week of August.

2. September 6, 2019: Standard protocol was implemented and notified to all medical officers, nursing staff, triage staffs and faculties who were working in the department. There were 35 medical officers and two faculties working at that time. Dissemination of protocol was done through department's web page (www.sites.google.com/pahs.edu.np/gpem), notice board of emergency department, handouts.

3. September 23, 2019 (Phase 2): Modified protocol was implemented to all medical officers, nursing staff, triage staffs and faculties who were working in the department. There were 35 medical

officers and two faculties working at that time. Dissemination of protocol was done through department's web page (www.sites.google.com/pahs.edu.np/gpem), notice board of emergency department, handouts.

4. September 30: Number of dengue patient started decreasing

Data was available in excel sheet. Data cleaning was done, which included changing Nepali date into English, adjusting age of all patients into years and data coding (e.g. Male =1, Female =1; Test positive =1 Test Negative =0) for analysis. A separate excel sheet labeled "Final Data" was prepared which contained; serial number, date, total number of patient each day, suspected dengue and highly suggestive dengue of each day. For the linearity of data moving average of total number of patient, suspected dengue and highly suggestive dengue was prepared in "Final Data".

Demographic variables were analyzed in excel sheet. Final data was transferred to SPSS 16.0. Variables was set as numerical. Date (September 1 to 30, 2019) will be considered as dependent variable, moving average of suspected dengue independent variables. Linear, cubic and quadratic curve fit module of was tested with ANOVA. P value of less than 0.05 will be taken as significant. The quadratic curve statistically significant so the equation this module was use to predict using regression analysis. Since standard protocol was applied from September 6 to 23, 2019, number of cases that would have been sent if standard protocol was continued beyond September 23 was calculated using regression equation. Similarly, total number of test that would have been sent if modified protocol had been used before September 23 was calculated using regression equation. The predicted value of suspected dengue was compared with actual value using T test.

Permission to use data has been taken from the Chair of department as standard protocol of the hospital. Names of patient was used for identification of the record and was not disclosed. Consent of patient was not possible as this is retrospective study. Data acquisition and analysis was started after obtaining approval from Institutional Review Committee, PAHS.

This methodology had some limitations. This study was conducted on the basis of available records, so sample and sample size and knowledge of medical person sending test is out of researcher's control. Data of the patient with fever whose dengue screening test was not sent was not available for the analysis. So, the trend of the highly suggestive dengue whose screening test was sent depends on the number of cases of suspected dengue.

RESULTS

Total of 10,773 patients visited emergency department of Patan Hospital from 15 August to 14 October 2019. Suspected dengue who presented with fever were 2567 (23.8%), out of which dengue screening test was positive in 658 patients. So, highly suggestive dengue was 6.1% of total patient and 25.6% of the suspected dengue. Minimum age of suspected dengue was 2 months and maximum age was 93 years (Table 1).

Table 1. Gender age of total patient(n=10,773) suspected dengue(n=2567), highly suggestive dengue (n=658)

	Total Patient	Suspected Dengue	Highly Suggestive
Male	5323 (49.4%)	1322 (51.5%)	346 (52.5%)
Female	5450 (50.6%)	1245 (48.5%)	312 (47.4%)
Average Age (Years)	26.1	25.7	27.4
Minimum Age (Years)	6 months	2 months	6 months
Maximum Age (Years)	93	93	86

Maximum (n=1854 i.e, 17.2% of total patient) number of patient flow was on Saturday of the week however screening test positive dengue was least on (n=73 i.e 11.09% of screening test positive patient) that day of the week (Figure 1).
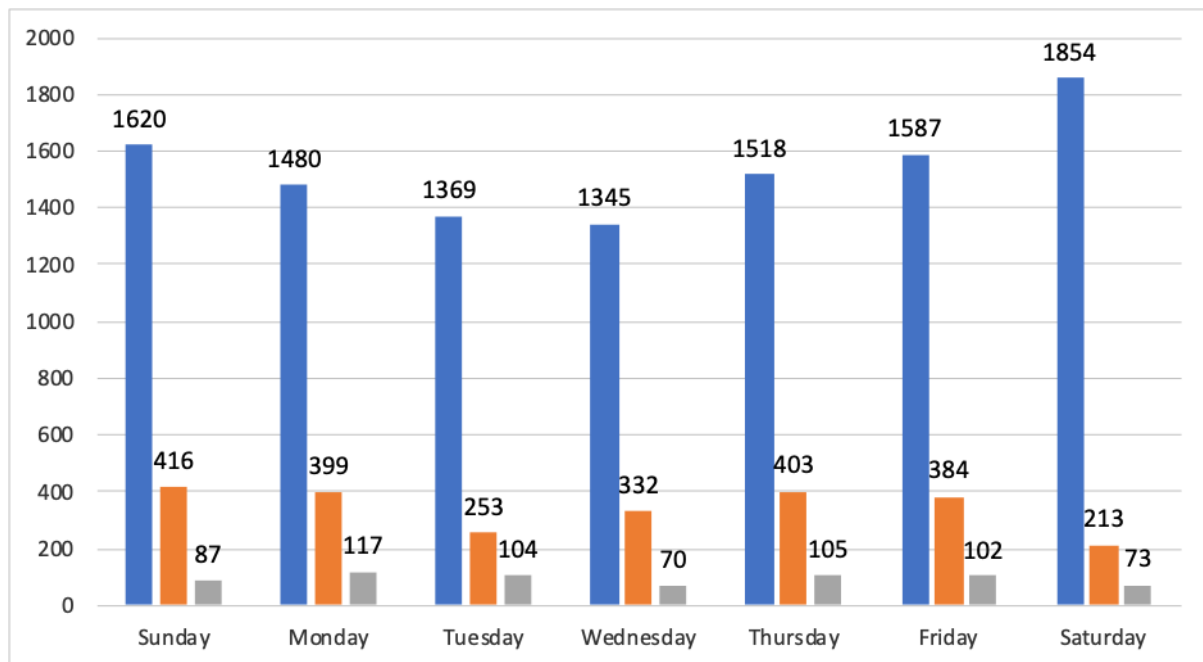
Figure 1. **Distribution of total patient(n=10,773) suspected dengue(n=2567), highly suggestive dengue (n=658) on weekdays and weekend**

The standard protocol was used in Phase 1 which was from September 6 to 23, 2019 (shaded area, figure 2) then after modified protocol was used.
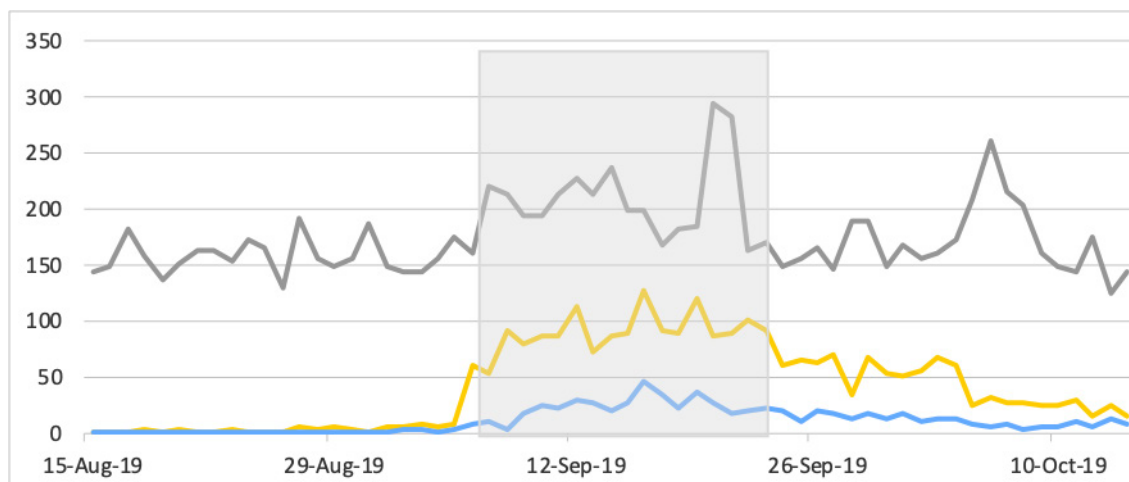

Figure 2. **Total patient(n=10,773) suspected dengue(n=2567), highly suggestive dengue (n=658) in time line**

*Brown line: Total patient; Yellow line: Suspected dengue; blue line: highly suggestive dengue; shaded area: period during which standard protocol was applied

Figure three shows the prediction of test sent in time series if modified protocol had been used from September 6, 2019. Median test sent per day was using standard protocol was 95.5 (IQR 89.4-98.2), if modified protocol had been used the median test would have been 89.0 (IQR 84.3-98.6), this was statistically significant (p=0.005).
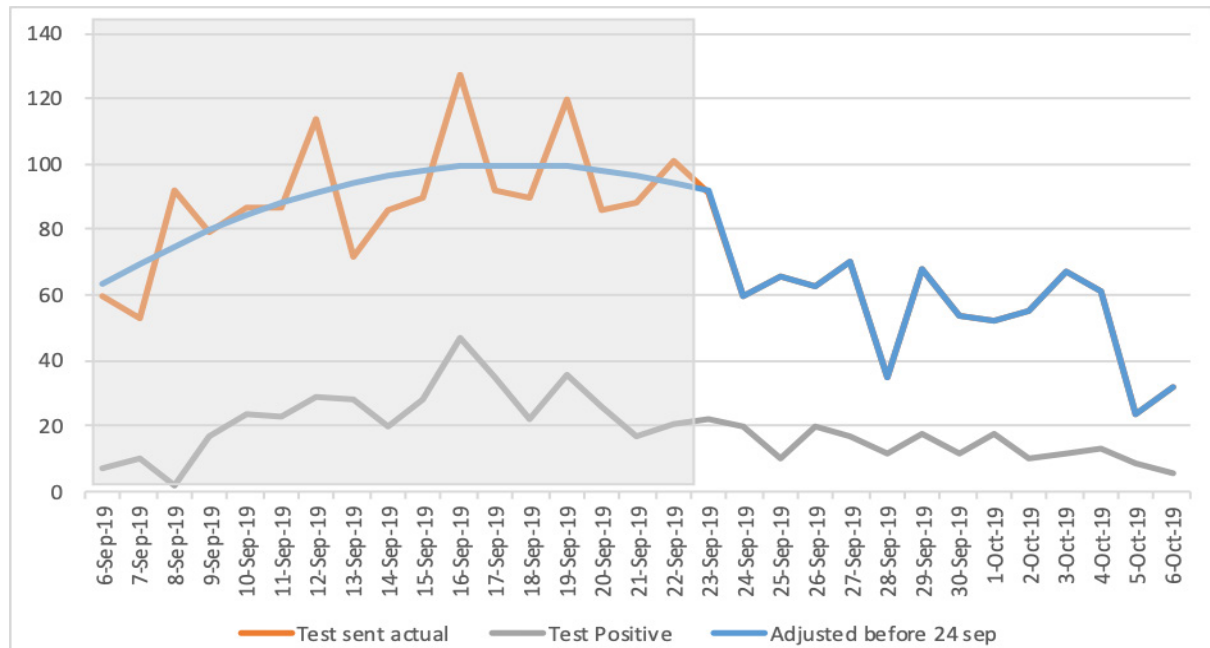
Figure 3. Prediction of test sent from September 6 to 23, 2019 if modified protocol had been used (Blue line) during that period

*Brown line: Highly suggestive dengue; Orange line: Test sent using standard protocol (standard protocol used till 23 September); Blue line (in shaded area): predicted test that would have been sent using modified protocol; Blue line (in non-shaded area): actual test sent using modified protocol

Regression equation was used to predict the number of test that would have been sent if standard protocol had been used after 23

September 2013 (Figure 4). In phase 2 median test sent per day using modified protocol was 60.5(IQR 52.5-66.8), if standard protocol had been continued median test would have been 61.0 (IQR 37.1-79.2)per day. It was not statistically significant (p=0.31).

Out of total 658 screening positive patients 454 (68.9%) had NS1 antigen positive, 197 (30%) had IgM positive and 7 (0.1%) had IgG positive.
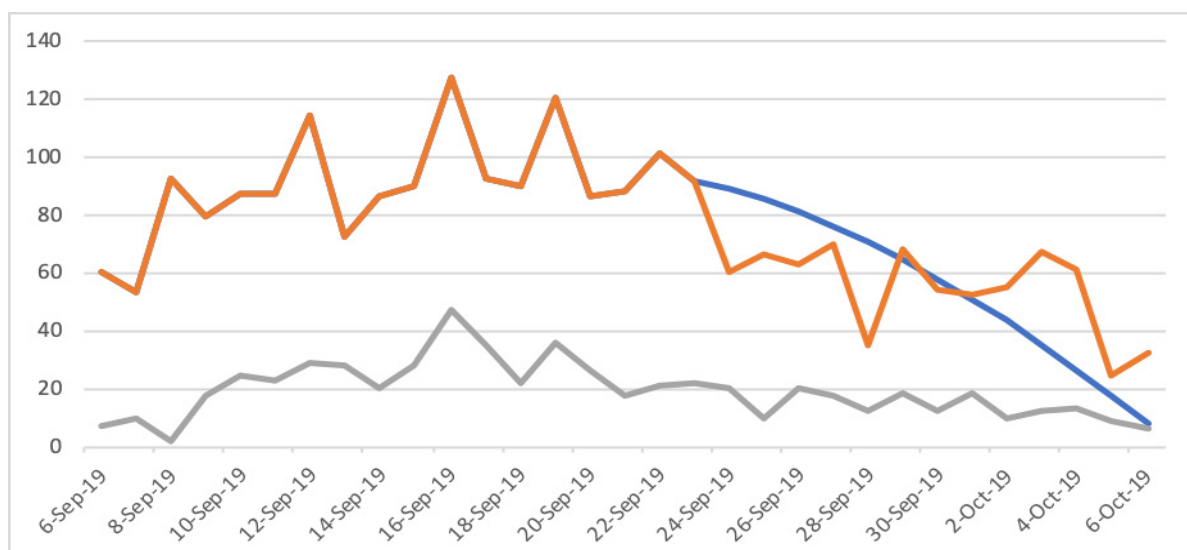

Figure 4. Prediction of test sent after September 23 if standard protocol had been used (Blue line)

*Brown line: Highly suggestive dengue; Orange line (Non – shaded): Test sent using standard protocol; Orange line (Shaded area): Test sent using modified protocol (started from 23 September); Blue line (shaded area): predicted test that would have been sent using standard protocol

DISCUSSION

Dengue screening is done with rapidly diagnostic test (RDT) which includes detecting NS1 antigen and IgM, IgG antibody against dengue virus.[3] Sensitivity and Specificity of a rapidly diagnostic test (RDT) varies from 55.3% to 91.7% and 85.3 to 98.5% and depends on timing of specimen collection and DENV serotype.[6] Clinical findings are also not specific for dengue diagnosis. A positive tourniquet test and absence of upper respiratory symptoms were two clinical findings that were independent predictors for laboratory-confirmed dengue. This study was however, conducted in children. The presence of two or more warning signs[7] was associated with a concurrent laboratory-confirmed diagnosis of severe dengue at hospital admission.[8]

We hypothesized that during epidemic the sensitivity and specificity of the diagnostic test remains same, however likelihood of clinical findings improves as more and more people gets affected with the disease. However, we did not find any literature to support this hypothesis. So, possibly clinical findings can be relied on more as outbreak progresses. So, during initial phase of outbreak when diagnosis is not clear it is running different test is essential to ensure safety of the patient, however as outbreak peaks, these tests can be minimized. This implies on yet another hypothesis that static protocols or guidelines are not useful. We need to have dynamic protocol which can be modified as per the load of the patient. This hypothesis is important to manage the surge of the patient during outbreak. Laboratory test requires substantial time to process and give report. If we can reduce the waiting time for laboratory result, the surge of the patient can be managed better. As shown in this study, implementing modified protocol will decreased the load of if it can be used early during the peak of outbreak.

Changing the protocol during epidemic may not always be feasible as there is very less time for orientation, so to analyze this, we did a curve fit module to find out the equation of the test sent using a standard protocol then we did predictive analysis to find out the number of investigation that would have been send if the same protocol had been used and compared it with the actual test sent. There was no significant difference between two. This showed that applying modified protocol did not change the number of test sent. However, it could have made difference if the both phases of protocol would have been mentioned in the outbreak plan and staffs were oriented to it. Change in plan needs to be oriented ahead of time. In Hongkong During the 2003 severe acute respiratory syndrome (SARS) crisis, we proposed and tested a new protocol for cardiac arrest in a patient with SARS. The protocol was rapidly and effectively instituted by teamwork training using high-fidelity simulation. It took two weeks for implementation.[9] So, this suggest that phase wise protocol needs to be oriented during inter epidemic period.

Then we did a retrospective predictive analysis to see what would be the number of test that would have been sent if we had used the modified protocol early in the timeline. This showed that less number of test would have been send with modified protocol and this was statistically significant. This shows that if we change protocol early during epidemic then the load of investigations that would have been sent will decrease. However, exact point of time for change of protocol is difficult to establish, so it needs to be decided on the basis of ground scenario, human resources and clinical judgment.

In our study, the number of patients did not vary according to the days in week, however during weekend, there was rise in total number of patient, this will affect those patients from outbreak. So, resource planning is another important issue that needs to be dynamic. The resource planned for weekdays might not be sufficient for weekend.

There is limitation of resources in any disaster or outbreak, so we need to manage our resource carefully. Protocol developed for case

management usually do not take into account the situation when there are more than expected number of cases and for many days. So, following protocol may cause increase waiting time for report and disposition. So, during the onset of outbreak, when disease condition is not clear and have wide differential, investigation should be done as per standard protocol. However, as day go by protocol needs to be modified considering the influx of patient.

CONCLUSIONS

Modifying protocol according to surge of patient during epidemic is helpful. Case management protocol needs to be dynamic to manage the surge of patient. It is difficult to find out the exact point of time from where protocol needs to be changed. Outbreak management plan and its training in inter epidemic period can be helpful.

CONFLICT OF INTEREST: None

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