



Seasonal Outbreak of Dengue Fever in Northern India - A Clinical Perspective and Predicting Length of Hospital Stay

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Authors' contributions

This work was carried out in collaboration between both authors. Author AC designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript. Author AK managed the analyses of the study. Both authors read and approved the final manuscript.

Article Information

DOI: 10.9734/IJTDH/2018/44585

Editor(s):

(1) Dr. Arthur V. M. Kwena, Professor, Department of Medical Biochemistry, Moi University, Kenya.

Reviewers:

(1) Lívia Garcia Bertolacci-Rocha, Universidade Federal de Goiás, Brasil.

(2) Jose Luis Turabian, Spain.

Complete Peer review History: <http://www.sciencedomain.org/review-history/26706>

Original Research Article

Received 25 July 2018
Accepted 09 October 2018
Published 19 October 2018

ABSTRACT

Aims: India reports frequent outbreaks of dengue fever every year. Scarcity of hospital beds during these outbreaks can be fatal to some. In this study we looked into the clinical and laboratory features of dengue fever in children and predictors of prolonged hospital stay.

Study Design: Prospective cross-sectional descriptive study

Place and Duration of Study: Department of Pediatrics, Hamdard Institute of Medical Sciences and Research from September to December 2017.

Methodology: This prospective study was conducted in admitted patients in the Pediatric department of a teaching hospital in Delhi to determine the clinical and laboratory features of all children admitted with dengue fever and find out any predictive factor for prolonged hospital admission. All clinical and laboratory confirmed dengue cases were included in the study. Patients were divided into dengue fever without warning signs (DF), dengue fever with warning signs (DWS) and severe dengue (SD) as per WHO Classification.

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Results: Of the 92 cases, 78 had positive IgM ELISA/NS1 Ag, 14 were clinical cases. The M:F is 1.7:1, the mean age is 7 ± 4.2 years. The common clinical features were fever (94%), abdominal pain (61%), vomiting (53%) and lethargy (52%). 61% patients were categorised as DWS, 30% as DF and 9% SD. The mean duration of hospital stay was 5 ± 2.8 days. 43% were hospitalised for > 5 days. Prolonged hospital stay (>5 days) was significantly associated with high grade fever ($>102^\circ\text{F}$) and lethargy ($p < 0.05$).

Conclusion: A high proportion of patients with DWS required hospitalisation. Admission during the critical phase of dengue is essentially life-saving. For clinical practice, the doctors working in the front line should be aware of the factors significantly prolonging LOS in the management of dengue fever. This can identify the patients at highest risks and help focus time and resources during seasonal outbreaks.

Keywords: Dengue fever; length of stay; lethargy.

1. INTRODUCTION

Dengue infection is a growing health problem all over the world. It is a mosquito-borne disease and has been inadvertently transferred from endemic region to many other parts of the world due to an increase in trade and tourism. The disease is widespread in the tropics, influenced by rainfall, temperature and unplanned urbanisation. According to World Health Organization (WHO), 40% of the world's population live in areas at risk of dengue transmission. In Asia, 1.8 billion people are at risk of dengue. In recent years, South-east Asia in particular, has seen large epidemics of Dengue virus infection with increasing mortality [1-2]. Dengue virus (DV) is a positive-strand RNA virus of the Flaviviridae family with 4 distinct serotypes (DV1-4). The virus is transmitted by *Aedes* mosquitoes. The clinical manifestations vary from mild constitutional symptoms to life-threatening conditions as dengue shock syndrome (DSS) and dengue hemorrhagic fever (DHF).

Epidemics in India have become frequent since the mid-1990s, especially in the urban areas. Since 1956, dengue virus infection has been reported in various parts of the country. The total number of Dengue cases have significantly increased in India since 2001 [3]. Many states in northern and southern India are now endemic to dengue infection. The expansion of dengue in India has been related to unplanned urbanisation, changes in environmental factors, host-pathogen interactions and immunological factors. In 2015, Delhi, India, recorded its worst outbreak since 2006 with over 15,000 cases [2].

The elucidation of the exact clinical profile is important for patient management and thus

crucial for saving life. Treatment is supportive. Outcome can be optimised by early recognition and cautious titrated fluid management [4]. In the present study an attempt is made to describe the salient clinical features in laboratory confirmed dengue fever in children admitted during the seasonal outbreak. Moreover, during these seasonal outbreaks, significant burden and stress are felt by the health care facilities. Dengue infection can have a bad outcome if not vigilantly screened and treated. Thereby identification of risk factors should be incorporated in the patient management protocols to provide better management. Moreover, the recent epidemiology in India has imposed significant economic and disease burden on patients and health care system with increased morbidity and hospital stay. This is of particular importance in a resource-limited setting. There is very little literature reporting on the length of hospital stay in dengue infections and the factors associated with prolonged hospital stay in the pediatric age group. Identification of the risk factors associated with prolonged hospital stay can help physicians to prioritise patient care. Moreover, during periods of outbreaks it helps the frontline resident and attending doctors to focus on appropriate admissions and allocate resources appropriately. Keeping this in mind, the present study was designed to look into the factors that prolong hospital stay in dengue infection.

2. MATERIALS AND METHODS

2.1 Design

The study is a hospital-based descriptive study with prospective data collection.

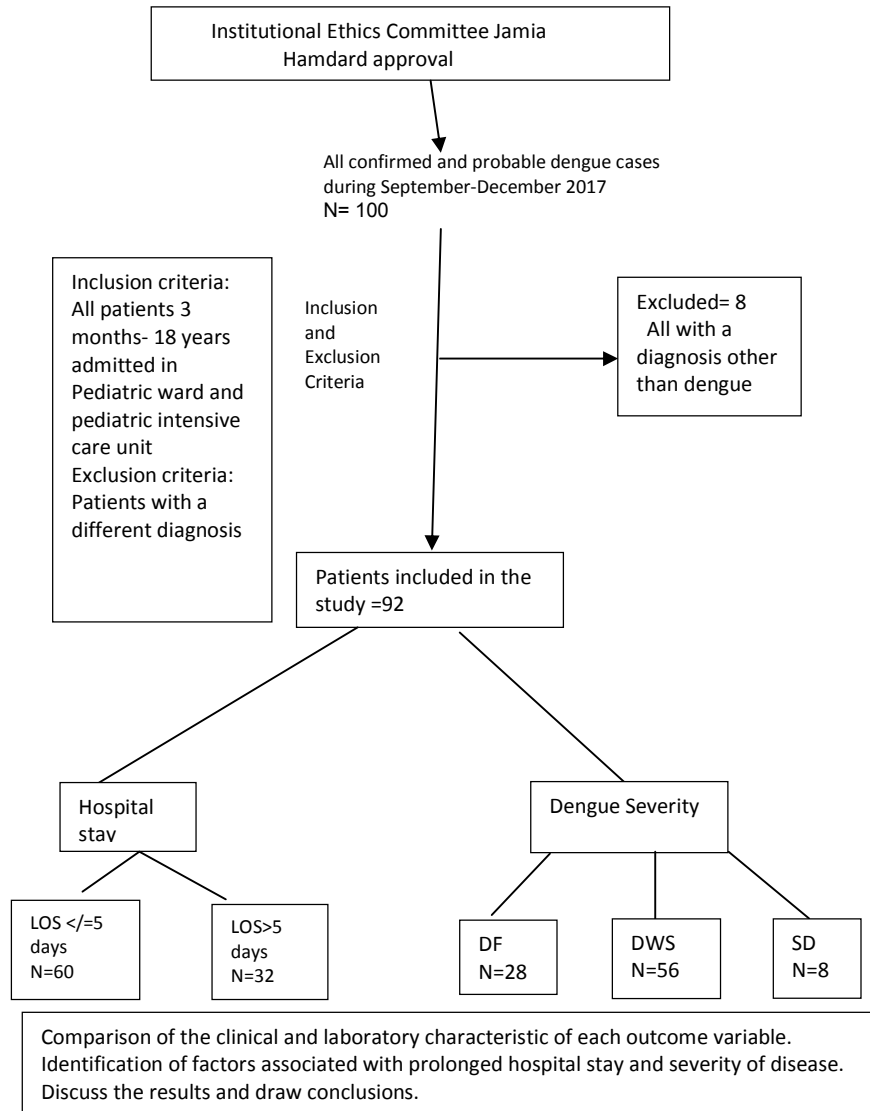


Fig. 1. Flow chart of methodology

2.2 Study Setting and Population

The study was conducted at Hamdard Institute of Medical Sciences and Research and associated HAHC Hospital, a tertiary-level teaching hospital located in the southern part of Delhi, India. All children aged 3 months-18 years admitted in pediatric ward with suspected and probable dengue were included in the study during the period September to December 2017.

2.3 Study Tools and Data Collection

The study group consisted of all children admitted in hospital with clinical features of

probable dengue as per WHO guidelines (2009). Suspected dengue infection was defined as the presence of fever and any two of the following symptoms: myalgia, headache, arthralgia, skin rash, retro-orbital pain, hemorrhagic manifestations(s), or leucopenia (white blood cell (WBC) count of $<4 \times 10^9 L^{-1}$). Patients were categorised as Dengue fever (DF), dengue with warning signs (DWS) and severe dengue (SD). Information was collected in a pre-structured questionnaire that was developed and based on review of literature. The study group represented the pediatric population. The study was conducted between 15th September 2017 to 31st December 2017 in the southern part of Delhi,

India. The patients were followed from the day of admission till discharge from hospital. All patients with probable and confirmed dengue were included in the study. The diagnosis of dengue fever, dengue with warning signs and severe dengue was based on the WHO criteria. All cases were tested for the presence of dengue immunoglobulin M and G antibodies in acute-phase serum by ELISA (Pan Bio Dengue IgM ELISA). The serum samples were also tested for dengue-specific NS1 in patients presenting within 5 days of fever (pan-E Early Dengue ELISA kit by Panbio). Patients with dengue infection have average hospital stay between 3-5 days [5-9]. We used >5 days as a cut-off for prolonged hospitalisation (the median hospital stay in our study was 5 days). Patients with a hospital stay of <5 days were compared with the patients with a hospital stay of >5 days to determine any predictors of prolonged hospital stay. Patients demographic and clinical features were recorded on the day of admission and the laboratory data were collected till the patient was discharged from hospital.

2.4 Definitions

Terms used in the current study were defined as follows.

Hospital stay is defined by ≥ 1 bed occupancy in hospital and mortality is death within 14 days after admission. > 5 days of hospital stay is defined as prolonged length of stay (LOS). Fever $>102^{\circ}\text{F}$ is defined as high grade fever. Thrombocytopenia is platelet count $< 100 \times 10^9$ cells. Hepatomegaly is defined as liver palpable below the right subcostal margin or the liver span

more than expected for age. Fluid accumulation is defined as any interstitial fluid accumulation (pleural effusion or ascites) proven by clinical and/or radiological examination.

3. RESULTS AND DISCUSSION

Of the total of 100 children admitted as suspected dengue, 8 patients were excluded. All excluded were diagnosed with other diseases. The final study group included 92 patients. Of the 92 cases, 78 (84.8%) were serologically confirmed and 14(15.2%) by the clinical criteria. There were 59(64.1%) males and 33(35.8%) females. Most of the patients were between 3 months-5 years (42%), 34% were between 6-10 years and 24% were above 11 years of age. The disease incidence amongst both sexes in the three age groups viz. 3 months-5, 5-10 and > 10 years showed a male preponderance (Fig. 2).

The patient’s mean age was 7.03 ± 4.25 years. The mean duration of symptoms before presentation to hospital was 4.76 ± 3.02 days (median 4, range 1-20days). The mean time to admission to hospital after onset of fever was 4 days. 72% of patients presented to hospital within 5 days of fever. The mean length-of-hospital-stay (LOS) was 5.1 ± 2.86 (median 5, range 1-20). 53% of patients were admitted for more than 5 days.

61% of cases were classified as dengue with warning signs (DWS), 30% dengue without warning signs (DF) while only 9% had severe dengue (SD). There were 2 deaths.

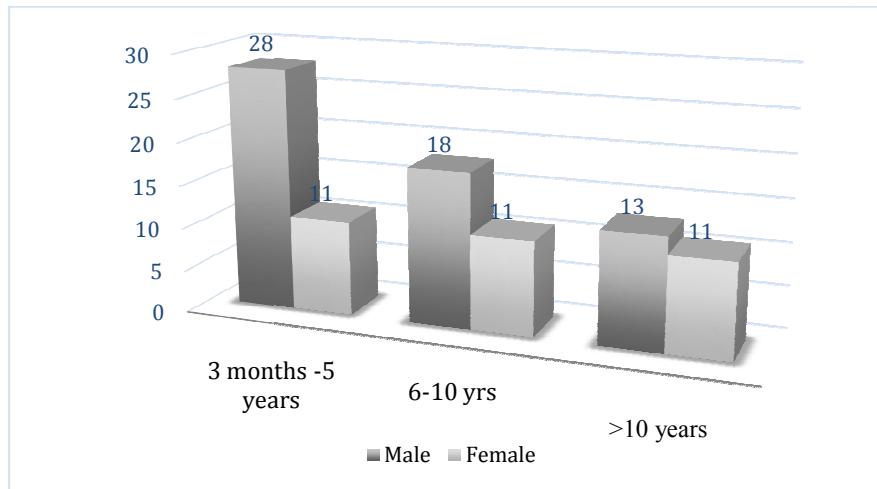


Fig. 2. Age and sex distribution

99% of patients documented fever. One patient (1%) without fever was febrile 2 days prior to admission. Fever >102°F was seen in 93.4% of patients. The predominant symptom was abdominal pain (60.8%) followed by vomiting (53.2%) and lethargy (52.1%). 26 % patients presented with body-ache while 18.4% patients presented with rash. Thrombocytopenia was seen in 53.2%, hepatomegaly in 42.3% and fluid accumulation (ascites/pleural effusion) was present in 31.5%. The other clinical manifestations include cough (19.5%) anorexia (16.3%), headache (11.9%), mucosal bleed (10.8%), nasal congestion (8.6%), dizziness (5.4%), chills (5.4%), eye pain (4.3%), and joint pain (2.1%) (Fig. 3).

Prolonged hospitalisation (>5 days) was seen in 53% (49/92) of patients while LOS was <5 days among 47% (43/92) of patients. The clinical characteristics of patients with or without prolonged LOS were compared (Table 1).

Prolonged hospitalisation was found to be significantly associated with high grade fever (>102°F) and lethargy (p<0.05).

The clinical characteristics of patient with varying degree of severity (DF, DWS and SD) were

compared (Table 2). SD was characterised with increased number of patients with <5 years old (75%), thrombocytopenia (87.5%), lethargy (100%), abdominal pain (87.5%), vomiting (87.5%), fluid accumulation (62.5%) and hepatomegaly (87.5%). These were found to be statistically significant (p<0.05).

Dengue fever is endemic in tropical Asia while India has seen an increased incidence of dengue fever in the past decade. The increase in dengue cases cause a substantial increase in the disease burden in terms of cost [10]. As stated earlier, during an outbreak scarcity of hospital beds due to increase number of cases can be fatal for some patients. This creates a lot of panic in the societal level during any outbreak season.

Identifying dengue patients with having high risk of prolonged hospital stay may help an effective measure in combating dengue-induced disease burden. There are very few studies on the predictors of prolonged hospital stay for dengue fever in children. We attempted to evaluate the factors associated with prolonged hospitalisation in children with dengue fever attending a tertiary care hospital.

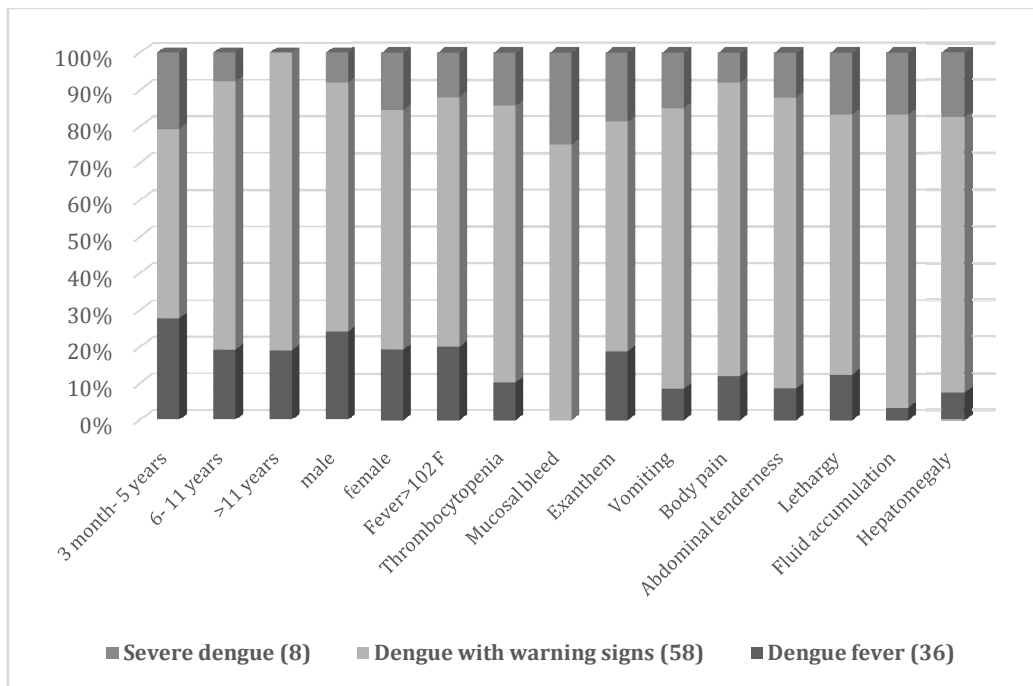


Fig. 3. Demographic and clinical features based on severity of illness

Table 1. Comparison of clinical characteristics of dengue patients according to presence or absence of prolonged hospital stay (>5 days)

Variables	Total cohort (n=92)	LOS in hospital		p Value*
		<5days (n=60)	>5days (n=32)	
Age (years), mean ± SD	7.03±4.25	6.99±3.99	7.11±4.77	0.957
< 5 years, n(%)	39(42.39%)	26(43.33%)	13(40.6%)	0.751
>5 years, n(%)	53(57.60%)	35(58.33%)	18(56.25%)	0.777
Male gender, n(%)	59(64.13%)	42(70.00%)	17(53.12%)	0.110
Dengue severity				
DF, n(%)	27(29.34%)	18(30.00%)	9(28.12%)	0.812
DWS, n(%)	56(60.87%)	36(60.00%)	20(62.50%)	0.890
SD, n(%)	2(2.17%)	2(3.33%)	0(0%)	0.539
Fever > 102°F, n(%)	57(61.96%)	32(53.33%)	25(78.12%)	0.017
Lethargy, n(%)	48(52.17%)	26(43.33%)	22(68.75%)	0.020
Vomiting, n(%)	48(52.17%)	31(51.67%)	17(53.12%)	0.746
Abdominal pain, n(%)	56(60.87%)	37(61.67%)	19(59.38%)	0.378
Mucosal bleed, n(%)	6(6.52%)	4(6.67%)	2(6.25%)	1.00
Hepatomegaly, n(%)	39(42.39%)	23(38.33%)	16(50.00%)	0.249
Fluid accumulation, n(%)	28(30.43%)	18(30.00%)	10(31.25%)	0.378
Thrombocytopenia, n(%)	49(53.26%)	32(53.33%)	17(53.12%)	0.919

*p values were calculated between patients with and without prolonged hospital stay LOS length of stay, DF dengue fever, DWS dengue fever with warning signs, SD severe dengue

Table 2. Comparison of clinical characteristics of dengue cases according to severity

	Dengue fever (28, 30.4%)	Dengue with warning signs (56, 60.8%)	Severe dengue (8, 8.7%)	p-value
3 month- 5 years, n (%)	8(28.6%)	15(26.8%)	6(75%)	0.009
6- 11 years, n (%)	5(17.9%)	19(33.9%)	2(25%)	0.376
>11 years, n (%)	4(14.3%)	17(30.4%)	0	0.115
Male, n (%)	12(42.9%)	34(60.7%)	4(50%)	0.628
Female, n (%)	5(17.9%)	17(30.4%)	4(50%)	0.628
Fever>102 F, n (%)	10(35.7%)	34(60.7%)	6(75%)	0.121
Thrombocytopenia, n (%)	5(17.9%)	37(66%)	7(87.5%)	<0.0001
Mucosal bleed, n (%)	0	6(10.7%)	2(25%)	0.0389
Exanthem, n (%)	3(10.7%)	10(17.9%)	3(37.5%)	0.238
Vomiting, n (%)	4(14.3%)	36(64.2%)	7(87.5%)	<0.0001
Body pain, n (%)	3(10.7%)	20(35.7%)	2(25%)	0
Abdominal tenderness, n (%)	5(17.9%)	46(82.1%)	7(87.5%)	<0.0001
Lethargy, n (%)	6(21.4%)	34(60.7%)	8(100%)	<0.0001
Fluid accumulation, n (%)	1(3.6%)	24(42.8%)	5(62.5%)	<0.0001
Hepatomegaly, n (%)	3(10.7%)	30(53.5%)	7(87.5%)	<0.0001

We have reported a seasonal outbreak of dengue fever in Delhi, which included 92 admissions of dengue fever in Hamdard Institute of Medical Sciences over a period of 4 months. In our study the mean age at presentation was 7 years in comparison with other studies [11]. Age group categorisation <5 years, 6-10 years and >11 years was done to look into the incidence and severity of the disease in each age category. The severity of dengue significantly increased with younger age (<5 years, p<0.05) as was seen in other Indian studies [12-16] though another study showed increased incidence in the adolescent group [16]. The study shows an

increased incidence of the disease in the male population in all the age categories as observed in another study [16]. Importance to a male child in the Indian culture and/or more covered dresses worn by girls may be the probable reason.

The average duration of hospital stay in our study was found to be 5 days. This is consistent with previous studies reporting mean hospitalisation between 3.4 and 6.2 days [5-9]. More than half of the studied population had a prolonged hospital stay which causes a substantial economic burden, both societal and

personal. Prolonged hospital stay was associated with DF and DWS, irrespective of severity which is in concordance with previous studies [17-18,19-22]. There was an equal distribution of the age groups among patients with or without a prolonged hospital stay. This study found no difference in LOS based on sex or age group. There is no previous study comparing this parameter in pediatric age group though Malhi et al. reported equal age distribution in a study where patients ≥ 12 years were included [23].

In our study it was seen that 60.8% patients were admitted with DWS while 8.7% were admitted with SD (Table 2). SD was more common (75%) in the younger age group (<5 years). This is in contrast to a previous study [6] where > 10-year-old age group was associated with severe disease. We found equal distribution of gender among the severe dengue patients. Patients with DWS are vulnerable to develop SD and complications of dengue fever. The proportion of severe cases is comparable with other studies [24]. This can probably be explained by the prevalent strain or the host interactions. As reflected in our study patients with DWS required admission for monitoring and supportive treatment. It could be concluded from our study that severe disease is seen in a younger age group (<5 years) and was significantly associated with lethargy, vomiting, abdominal tenderness, hepatomegaly and fluid accumulation [6].

3.1 Study Limitations

Several shortcomings of the present study should be considered. This is a single centre paediatric study, so the results should not necessarily be generalised to adult population. Additionally, the study sample includes the patients admitted based on the clinician's assessment. This can vary among various clinicians attending the patients and may interfere with the results of our findings. However, the admission criteria was based on the WHO 2009 dengue guidelines. The study population may be underrepresented if some patients refused admission for various reasons or overrepresented if admissions were not correctly justified.

The strength of this study lies in our attempt to study this cohort of dengue patients. This study is able to improve the awareness of prolonged hospital stay and dengue severity. The study also brings forth the need for more studies and

help strategise protocols to fight the disease burden during outbreaks.

4. CONCLUSION

It can be concluded that the younger age group, high grade fever and lethargy is associated with prolonged hospitalisation. Early identification of dengue patients with these factors can probably be of advantage in terms of appropriate decisions about treatment and management in high dependency units. Dengue-related bed occupancy and mortality may be reduced if due attention to the high risks patients are given, thereby making a positive impact on both patients and healthcare system.

CONSENT

All authors declare that 'written informed consent was obtained from the patient (or other approved parties) for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editorial office/Chief Editor/Editorial Board members of this journal.

ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Peer-review history:
The peer review history for this paper can be accessed here:
<http://www.sciencedomain.org/review-history/26706>