Original Article

A MATCHED CASE – CONTROL STUDY TO IDENTIFY POTENTIAL RISK FACTORS OF DENGUE FEVER AMONG RESIDENTS OF A LOCAL UNIVERSITY, LAHORE

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Abstract

Objective: To identify potential risk factors of dengue fever (DF).

Study Design: 1:1 matched case-control study.

Methodology: Cases were those participants confirmed with DF by laboratory investigation (n = 37) and controls (n = 37) were selected from participants who had no past history of having DF during their stay at the city campus of University of Veterinary and Animal Sciences, Lahore during the outbreak of 2010 and 2011 and were matched on education level.

Data Analysis: Logistic regression analyses were applied to check the association of risk factors with dengue infection.

Results: Signs and symptoms showed that the patients suffering from DF had fever (100%), headache (100%), body pain (97.3%), eye pain (89.2%), joint pain (83.8%), abdominal pain (62.2%), gum bleeding (37.8%), nasal bleeding (18.9%), diarrhea (27%), blood in stool (5.4%) and blood in urine (2.7%). People not using repellents (Odds Ratio [OR] = 6.68; 95% Confidence Interval [CI]: 1.30 – 34.18), and people not sleeping inside screened doors and windows (OR = 4.82; 95% CI: 1.17-19.72) were the significant potential risk factors.

Conclusion: Dengue could be controlled by awareness and adapting protective measures.

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Introduction

Dengue Fever (DF) / Dengue Hemorrhagic Fever (DHF) is a significant threat to public health due to high morbidity and low mortality worldwide. Being one of the most important and frequent mosquito-borne viral infections of human, characterized by sudden fever, severe headache, rashes, muscle pain, retro-orbital pain, leucopenia, nausea, vomiting, lack of appetite, taste disturbance and general weakness and sometime petechial bleeding.[1] It is caused by RNA virus belonging to genus *Flavivirus* of family *Flaviviridae*, transmitted by the bite of female mosquito *Aedes aegypti* (*A. aegypti*) and *A. albopictus.*[2] The mosquito may bite at any time but the probability of being bitten increases at dusk and dawn.[3] Female *A. aegypti* mosquitoes interact closely with humans, as they need human blood to live and to fertilize their eggs. The four antigenically distinctive serotypes of DF virus are; DEN_1, DEN_2, DEN_3 and DEN_4.[4] The virus completes its growth phase in the *Aedes aegypti* gut and then moves to the salivary glands of the mosquito. The virus is inoculated subcutaneously to healthy person through the bite of infected mosquito.[5]

At present, no licensed vaccines or specific drugs are available moreover substantial vector control efforts are also not efficient to control rapid emergence and spread of the disease. The contemporary worldwide distribution of dengue infection and its public health impact are poorly known.[6]

As DF is considered as one of the most important vector – borne disease of public health significance,[7] millions of cases of DF and DHF are reported every year in the tropical regions of America, Africa, Asia and Oceania.[8] Approximately 2.5 billion people worldwide are exposed to the risk of DF and its severe forms; DHF and Dengue Shock Syndrome (DSS) and among those; about 75% (approximately 1.8 billion) live in the Asia – Pacific Region. Approximately 50 million cases of DF occur worldwide and nearly 0.5 million people suffering from DHF require hospitalization annually. Children especially less than five years of age are the most affected (approximately 90%) population from among the total infected. Nearly 2.5% of those affected by dengue infection die due to the disease.[9] Initial epidemics of DF were reported in 1779 – 1780 in Asia, Africa, and North America. A large pandemic of dengue infection started in Southeast Asia just after World War II and amplified during the last 15 years.[10]

Prevention and control of DF and DHF depends on active as well as passive surveillance programmes. The aims of these programs lie in the early detection of outbreaks along with the speedy application of control measures.[11]

In Pakistan, the 1st confirmed outbreak of DHF occurred due to serotype DEN_2. This outbreak was reported by Aga Khan University Hospital (AKUH) in June 1994.[12] Afterwards, increased numbers of DHF cases have been reported throughout the country. Out of four serotypes of DF virus, two serotypes i.e. DEN_1 and DEN_2 have been detected in the sera of children having unknown fever.[13] In the year 1998, simultaneous circulation of DEN_1 and DEN_2 caused an outbreak of DF in the Baluchistan province.[14] In 2005, a large number of serotype DEN_3 DHF cases was reported in several hospitals of Karachi[15]. Thereafter, in 2006, approximately 3,640 cases of DHF due to serotypes (DEN_2 and DEN_3) were identified in different hospitals throughout the country.[16]

Keeping in view the regular occurrence of the disease the present study has been planned with the objective to identify potential risk factors associated with the DF among the residents (students and staff members) of University of Veterinary and Animal Sciences (UVAS), Lahore, Pakistan.

Materials and Methods

Lahore is the second biggest city of Pakistan, which has a total land area of the city is 404 sq. km. The Ravi River flows across the north of Lahore. Altitude of the city lies between 31°15 and 31°45 North latitudes and 74°01 and 74°39 East longitudes. The population of Lahore enjoys four seasons round the year. May, June and July are the hottest months while three months namely; December, January and February are the coldest months.[17]

Study Design

A case – control study matched on 1:1 ratio of cases and controls was conducted at the city campus area of UVAS, Lahore, Pakistan during the month of May 2013. The total population of the city campus of university was 3820, which included student, teaching and non-teaching staff. Initially a survey was conducted at the campus area and persons infected with DF during the outbreaks of 2010 and 2011 were identified. A list was prepared and all cases (n = 37) were included in the study. Healthy controls (n = 37) matched on

education level with cases were also selected from the same population, who were negative for the disease during that period. A total of 74 individuals were selected for the study.

A case was defined as a person who had suffered from DF / DHF during any of the two epidemics in Lahore in 2010 and 2011 and was residing at the university campus during this period. A control was also a single person who did not suffer from DF or dengue like illness during 2010 and 2011 and was residing on the same campus.

Statistical Analysis

Data about demographic characteristics of study subjects e.g. sex, age, monthly income etc. and potential risk factors was collected on a pre-designed questionnaire in a face to face interview with the selected cases and controls after seeking formal consent. Conditional logistic regression was applied to see the association of the factors with dengue infection. Statistical analysis was conducted in the *R* statistical software.[18] Univariable analysis was conducted for initial screening of variables. Potential risk factors, for whom the p-value was < 0.25 were further carried forward for inclusion in a multivariable regression analysis. A forward stepwise variable – selection strategy[19] was adopted to develop the final model. P-value < 0.05 was considered statistically significant.

Ethical Consideration

Every study participant was explained about the aims and objectives of the study and informed consent was also obtained from the participants for publication of information. During interview, cases and controls were assured anonymity and confidentiality about their data.

Results

Signs and symptoms showed that all the patient who suffered from DF/DHF, had fever and headache; Other common symptoms included body pain (97.3%), eye pain (89.2%), joint pain (83.8%), abdominal pain (62.2%) and bleeding gum (37.8%), nasals bleeding (18.9%), diarrhea (27%). While blood in stool (5.4%) and blood in urine (2.7%) was rarely present.

In the univariable analyses, 12 variables were initially screened and 4 variables were found to be associated with the being a case or control i.e. ($p < 0.25$), which include, not using repellent, not using nets, not sleeping inside screened doors and windows, and not using chemicals and sprays (Table 1). All these factors were found to be risk factors (OR > 1.00). People who did not use repellents were also more likely to become positive cases as compared to those who used the repellents (OR = 6.00; 95% CI: 1.34 – 26.81; p-value = 0.019). The odds of not using nets were 3 times higher (95% CI: 0.81 – 11.08; p-value = 0.0994) among cases than control. The odds of not living inside houses with screened doors and windows were 4.33 times higher (95% CI: 1.23 – 15.21; p-value = 0.0221) among cases than control. Avoiding chemicals use to kill larvae of mosquitoes enhanced the likelihood of dengue infection by 8 times (95% CI: 1.00 – 63.96; p-value = 0.0499) in univariable analysis.

No association was found between dengue infection and people not using nets during sleeping (p-value = 0.0994). Other factors like age (p-value = 1), sex (p-value= 0.999), monthly income (p-value = 0.671), presence of a member in the family who suffered from dengue (p-value = 0.796), wearing half sleeves shirts (p-value = 0.763), presence of pond in the vicinity of the house (p-value = 1), and space spray used by the participants were found insignificant (p-value = 1).

Table 1: Results of univariable conditional logistic analysis of the possible factors associated with the increased risk of dengue infection.

Variable Name	Case (%) (n = 37)	Control (%) (n = 37)	Odds Ratio	95% CI	p-value
Not using repellent	26 (70.27)	16 (43.24)	6.00	1.34 – 26.81	0.0190
Not using nets	34 (91.89)	28 (75.68)	3.00	0.81 – 11.08	0.0994
Not sleeping inside screened door and windows	16 (43.24)	6 (16.22)	4.33	1.23 – 15.21	0.0221
Not using chemicals and sprays	24 (64.86)	17 (45.95)	8.00	1.00 – 63.96	0.0499

Table 2: Results of final conditional logistic model with potential risk factors of Dengue infection.

Variable Name	Adjusted Odds Ratio	95% CI	p-value
Not using repellents	6.68	1.30 – 34.18	0.0226
Not sleeping inside screened doors and windows	4.82	1.17-19.72	0.0286

The final model with conditional logistic regression identified 2 variables as potential risk factors (Table 2). These included people not using repellents (OR = 6.68; 95% CI: 1.30 – 34.18; p-value = 0.0226) and people not sleeping inside screened doors and windows (OR = 4.82; 95% CI: 1.17 – 19.72; p-value = 0.0286).

Discussion

The results of our study showed that there was a significant association between dengue infection and people who did not use repellents against mosquitoes (OR = 6.68; 95% CI: 1.30 – 34.18; p-value = 0.0226) compared to those who used the repellents. Contrary to our results, no association was seen between using repellent and DF in another study.[20]

The likelihood of becoming a DF patient among people, not living inside houses with screened doors and windows, was 4.82 times higher than those people who were sleeping inside screened doors and windows houses (95% CI: 1.17 – 19.72). Similar finding were also reported in a study conducted in Johor Bahru, Malaysia (OR = 4.2; 95% CI: 1.02 – 29.03).[20] Another study conducted in Taiwan revealed the use of screened windows and doors very effective against *Aedes spp* bite, thus reducing the risk of DF (odds ratio adjusted from 0.18 (95% CI: 0.06 – 0.56) to 0.58 (95% CI: 0.36 – 0.92).[21]

Avoiding the use of mosquito nets in the areas, were found non-significant (p-value > 0.05). Contrary to this, studies in India have shown that mosquito nets give best protection from mosquitoes than the use of other repellents and coils.[22] Avoiding the anti-mosquitoes chemicals to kill larvae enhanced the likelihood of becoming a case by 8 times (95% CI: 1.00 – 63.96) compared to those who used chemicals. Space sprays with insecticides to kill adult mosquitoes are not usually effective[11,23] unless they were used indoors. Due to behavior and close association of vector with humans, *A. aegypti* generally required the use of a combination of vector – control techniques, most notably environmental management methods as well as chemical methods, which are based on the use of larvicide and adulticide sprays.[24]

Sex of the participants did not show any significant association with dengue infection while contrary to these results, studies in India and Singapore reported that dengue was more prevalent in males than females.[25,26] No association was found between dengue illness and wearing of half sleeves shirts by the participants, these results were contrary to results of other studies which reported that wearing full sleeves or more than one pair of clothes remained protective against dengue.[20] Our results might have been affected by the small sample size i.e. 37 cases only. While the studies conducted in Singapore, comprised of 206 patients,[25] in Europe, data of 309 participants was reported[26] and data of 154 cases and control was presented in a study conducted in Johor Bahru.[20]

Conclusion

This study was conducted to find association between DF and potential risk factors among the residents of University of Veterinary and Animal Sciences, City campus, Lahore, Pakistan. There are several factors like not using screened doors and windows and not using repellents, which are significantly associated with enhancing the exposure to DF. By adopting protective measures, future outbreaks can be controlled. Enhanced sanitary practices and awareness of masses could further reduce the risk.

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