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Original Article

Respiratory symptoms: a significant factor to be considered in dengue infection

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Abstract

Introduction: Dengue is a major arboviral infection. Clinical manifestations range widely from mild, non-specific febrile syndromes to serious, life-threatening conditions. Dengue cases have increased globally over the last ten years. Dengue patients show gastrointestinal and respiratory symptoms. The aim of this study was to identify the associated demographic risk factors, and evaluate the significance of respiratory symptoms for early diagnosis.

Methodology: Blood samples were collected from dengue-suspected patients reported to various health centers in South Andaman, from January 2018 to December 2022, and were processed by antigen/antibody assay. The odds of factors for being dengue positive among dengue suspects were analyzed using the Chi-square test, logistic regression models, and random forest analysis.

Results: Blood samples were collected from 14,783 (99.6%) of the 14,836 dengue suspects. Dengue infection was confirmed in 1,354 (9.2%) suspects. A significantly higher prevalence of infection was observed in the age group 16 to 30 years. Resident males of urban areas had higher dengue positives. Fever was a significant clinical manifestation of dengue infection. Rhinorrhea and other respiratory symptoms showed a significant association ($p < 0.05$) with dengue infection.

Conclusions: Respiratory discomfort was found to have a significant association with individuals suspected of dengue. Dengue positivity rate per 1000 population was high among these individuals. This study determined the key signs that can be considered significant to suspect dengue, including respiratory ailments. This will help the healthcare professionals to identify dengue cases at an early stage, to initiate fluid-based treatment.

Key words: risk-factors; dengue; hemorrhage; respiratory; South-Andaman.

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Introduction

Dengue fever/dengue hemorrhagic fever (DF/DHF) is an infectious disease, the causative agent (virus) of which is transmitted by mosquitoes. The dengue virus (DENV) is classified into four distinct serotypes: DENV-1, DENV-2, DENV-3, and DENV-4 [1]. The mode of transmission is primarily through the infective bite of mosquito vectors *Aedes aegypti* and *Aedes albopictus* [2]. It has recently been reported that DF/DHF is prevalent in various tropical and sub-tropical regions of the globe, and causes significant economic burden [1,3]. According to estimates of the World Health Organization (WHO), approximately 50% of the global population is currently susceptible to DF/DHF, with an annual incidence of 100–400 million cases [4].

In India, DF/DHF emerged as a significant public health concern due to high morbidity and mortality rates [5,6]. Developing countries such as India, China, and Brazil have experienced a significant number of outbreaks [7,8]. The Indian subcontinent has favorable climatic conditions for the transmission of dengue virus by mosquitoes leading to the occurrence of multiple epidemic outbreaks annually [9]. Different serotypes of DENV have been circulating in India since 1963, resulting in numerous epidemics every year. Furthermore, more than 100,000 dengue cases occur in India each year, resulting in 200 to 400 deaths [9].

The treatment of dengue is primarily based on symptoms. India is yet to consider the ongoing available phase–3 tetravalent vaccines that could play a significant role in the prevention of DF/DHF. The Ministry of Health and Family Welfare, India is actively involved in conducting clinical trials related to DF/DHF prevention and treatment [10]. In spite of these efforts, factors such as urbanization leading to proliferation of artificial breeding habitats [11–14], lack of medical infrastructure [14,15], and lack of access to healthcare have contributed to an underestimation of dengue cases [16]. The Andaman and Nicobar Islands consist of many remote and isolated islands, making it difficult for patients to access healthcare services consistently due to the limited connectivity [17].

DF/DHF is a significant public health concern in Andaman and Nicobar Islands due to its endemic-epidemic pattern. The DENV1 and DENV2 serotypes

were observed in this island along with DF/DHF in 2009. Havelock Island experienced DENV3 outbreak in 2014, and subsequently DENV4 was reported during 2018 [18–21]. Simultaneous circulation of all serotypes within the islands led to an increase in DF and DHF [18] over these years, as observed in the reports of the Integrated Disease Surveillance Program (IDSP) [22].

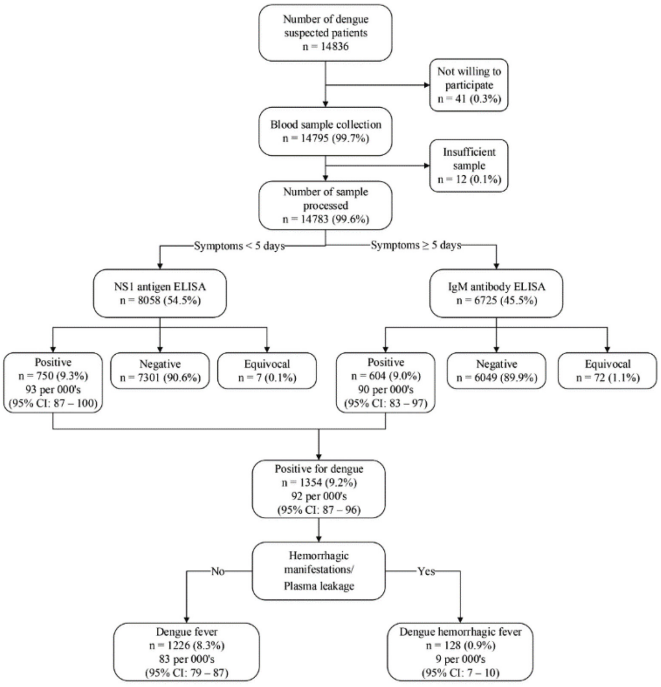
Investigation on the suspected cases of dengue is important. Identification of significant factors which define a typical dengue case can reduce the time required for diagnosis, and thus lessen the overall burden of dengue [23,24]. This study focused on identifying the key risk factors for DF/DHF which will aid in early diagnosis. The pattern of symptoms on the demographic diversity of DF/DHF was also explored.

Methodology

Study design and participants

The study was carried out in the health facilities of South Andaman, Andaman and Nicobar Islands between January 2018 and December 2022. The study subjects included those who visited the health facilities (district hospital, community health centers, and primary health centers) and were suspected of dengue. The patients suspected of dengue by the physician were referred to the laboratory of the health facility to draw blood for further testing and analysis. As per the World Health Organization, dengue can be suspected in those with one or more symptoms, including; fever with a temperature of 40 °C / 104 °F, headache, eye pain, joint pain, nausea, vomiting, swelling and rash.

Figure 1. CONSORT diagram: Participant disposition flowchart for the study.



The study participants aged between 1 month and 99 years were evaluated for the presence of respiratory signs and symptoms such as cough, sore throat, and rhinorrhea. A standardized proforma was used to collect data on demographics, gastrointestinal conditions, respiratory conditions, and recent travel history, including any trips outside the participant's primary residential area within the past two weeks. Blood was collected from the participants and transported to the testing facility in cold chain. The serum was separated and tested for the presence of dengue specific antigen/antibody. The participant's information was gathered after obtaining prior informed consent. The data collected from the study participants were kept confidential. The study was approved by the institutional human ethics committee.

Laboratory diagnosis

Blood samples were collected from patients within 5 days of symptom onset for NS1 antigen detection using the Panbio Dengue Early ELISA (Abbott Panbio Dengue Early ELISA, catalogue number 01PE40, Abbot Panbio USA). The samples were collected 5 days post-illness onset for IgM antibody detection, and tested using a DENV IgM capture ELISA [18–21,25,26]. A positive result in either test confirmed dengue infection [27].

Patient serum was added to microtiter plate wells coated with dengue polyclonal anti-NS1 antibody. After incubation and washing, horseradish peroxidase (HRP)-conjugated anti-NS1 monoclonal antibody (Mab) was added, followed by 3,3′,5,5′-tetramethylbenzidine (TMB) substrate. The optical density (OD) was measured at 450 nm. An index value was calculated to determine the test result: < 0.9 negative, 0.9–1.1 equivocal, and > 1.1 positive.

Serum samples were diluted and added to pre-coated wells for IgM antibody detection. DENV antigen, anti-DENV monoclonal antibody, and avidin-HRP were sequentially added and incubated. TMB substrate was added, and the OD was measured at 450 nm.

Classification of dengue fever and dengue hemorrhagic fever

Dengue fever is characterized by two or more clinical manifestations in febrile patients. The clinical presentation includes signs and symptoms such as leukopenia, myalgia, arthralgia, rash, nausea, and vomiting. DHF is defined by any of these symptoms,

along with significant plasma leakage, which causes shock or fluid accumulation, as well as respiratory distress, severe bleeding, organ dysfunction, altered consciousness or heart dysfunction [28].

Data analysis

A database was created using Microsoft Excel 2016 (Microsoft Corporation, Albuquerque, NM, USA) to compile and prepare the data for analysis. The data was rigorously verified and processed to ensure completeness and logical validity. Subsequent statistical analyses were conducted using STATA version 15.1 (StataCorp, Texas, USA). Descriptive statistics were employed to summarize the data, including frequency and percentage for categorical variables, and median with interquartile range for non-normally distributed continuous variables. Mean and standard deviation were used for normally distributed continuous variables. The crude dengue positivity rate was calculated per 1000 population. The Chi-square (χ^2) tests were used to assess the association between factors and dengue positivity. The Fisher's exact test was applied in the case of factors that had fewer than 5 observations. Logistic regression models, both simple and multiple, were employed to determine the odds of dengue positivity associated with demographic, respiratory, and dengue symptoms. Given the multiple significant factors identified, random forest (RF) analysis was performed to rank the importance of respiratory and dengue symptoms in classifying dengue positivity among suspects. All statistical tests were two-tailed with a significance level of 0.05.

Results

A total of 14,836 suspected dengue cases were contacted and blood samples were collected from 14,783 (99.7%) individuals. Of these, 8,058 (54.5%) had symptoms for less than 5 days and hence were tested for the NS1 antigen. An IgM enzyme-linked immunosorbent assay (ELISA) test was performed on all patients who reported ill for more than 5 days (n = 6,725; 45.5%). Among the samples tested, 1,354 samples (16.4%) were positive for dengue, which corresponds to an estimated positivity rate of 92 cases per thousand (95% CI: 87–96). There were 604 (9.0%) who tested positive for IgM antibody ELISA and 750

Table 1. Factors associated with dengue fever and dengue hemorrhagic fever.

Characteristics	Sampled [N = 14783]		Dengue positive [n = 1354]		Positivity rate per 000's (95% CI)
	n	%	n	%	
Age (years)					
≤ 15	4,269	28.9%	426	31.5%	100 (91, 109)
16–30	4,355	29.5%	500	36.9%	115 (105, 125)
31–45	3,376	22.8%	276	20.4%	82 (73, 92)
> 45	2,783	18.8%	152	11.2%	55 (46, 64)
p value			< 0.001		
Gender					
Male	7,927	53.6%	796	58.8%	100 (94, 107)
Female	6,856	46.4%	558	41.2%	81 (75, 88)
p value			< 0.001		
Residential area					
Rural	6,207	42.0%	412	30.4%	66 (60, 73)
Urban	8,576	58.0%	942	69.6%	110 (103, 117)
p value			< 0.001		
Having household members with similar health problems					
No	9,606	65.0%	628	46.4%	65 (61, 71)
Yes	5,177	35.0%	726	53.6%	140 (131, 150)
p value			< 0.001		
Do you know any members in your village or locality with similar health problems?					
No	10,047	68.0%	669	49.4%	67 (62, 72)
Yes	4,736	32.0%	685	50.6%	145 (135, 155)
p value			< 0.001		
Have you travelled anywhere out of Island in the last seven days?					
No	9,941	67.2%	652	48.2%	66 (61, 71)
Yes	4,842	32.8%	702	51.8%	145 (135, 155)
p value			< 0.001		
Severity of respiratory symptoms					
Nil	11,406	77.2%	338	25.0%	30 (27, 33)
One	1,112	32.9%	268	19.8%	241 (216, 267)
Two	1,017	44.9%	286	21.1%	281 (254, 310)
≥ Three	1,248	35.7%	462	34.1%	370 (343, 398)
p value			< 0.001		
Severity of dengue symptoms					
Nil	**2,244**	**15.2%**	**208**	**15.4%**	**93 (81, 105)**
One	3,380	27.0%	202	14.9%	60 (52, 68)
Two	6,251	68.2%	408	30.1%	65 (59, 72)
≥ Three	2,908	100.0%	536	39.6%	184 (170, 199)
p value			< 0.001		

The table depicts the association of dengue with demographic characteristics among the dengue suspects in the study area.

(9.3%) tested positive for NS1 antigen ELISA. Dengue hemorrhagic fever (DHF) was observed in 128 patients (9.5%) (Figure 1).

The positivity rates were higher in the urban population (110; 95% CI: 103, 117) and in the male gender (100; 95% CI: 94, 107). The severity of the

Table 2. Respiratory and dengue symptoms associated with the dengue fever (DF) and dengue hemorrhagic fever (DHF) among the dengue suspects.

Symptoms	Sampled [N = 14783]		Dengue positive [n = 1354]		Positivity rate per 000's (95% CI)	DF positive [n = 1226]		Positivity rate per 000's (95% CI)	DHF positive [n = 128]		Positivity rate per 000's (95% CI)
	n	%	n	%		n	%		n	%	
Having cold											
No	12,907	87.3%	729	53.8%	56 (53, 61)	682	55.6%	53 (49, 57)	47	36.7%	4 (3, 5)
Yes	1,876	12.7%	625	46.2%	333 (312, 355)	544	44.4%	290 (270, 311)	81	63.3%	43 (34, 53)
p value			< 0.001			< 0.001			< 0.001		
Having cough											
No	12,527	84.7%	650	48.0%	52 (48, 56)	621	50.7%	50 (46, 54)	29	22.7%	2 (2, 3)
Yes	2,256	15.3%	704	52.0%	312 (293, 332)	605	49.3%	268 (250, 287)	99	77.3%	44 (36, 53)
p value			< 0.001			< 0.001			< 0.001		
Having dry cough											
No	14,516	98.2%	1257	92.8%	87 (82, 91)	1169	95.4%	81 (76, 85)	88	68.8%	6 (5, 7)
Yes	267	1.8%	97	7.2%	363 (306, 424)	57	4.6%	213 (166, 268)	40	31.3%	150 (109, 198)
p value			< 0.001			< 0.001			<0.001		
Having congestion in nose											
No	14,382	97.3%	1269	93.7%	88 (84, 93)	1196	97.6%	83 (79, 88)	73	57.0%	5 (4, 6)
Yes	401	2.7%	85	6.3%	212 (173, 255)	30	2.4%	75 (51, 105)	55	43.0%	137 (105, 175)
p value			< 0.001			0.550			< 0.001		
Having running nose											
No	13,182	89.2%	682	50.4%	52 (48, 56)	619	50.5%	47 (43, 51)	63	49.2%	5 (4, 6)
Yes	1,601	10.8%	672	49.6%	420 (395, 444)	607	49.5%	379 (355, 403)	65	50.8%	41 (31, 51)
p value			< 0.001			< 0.001			< 0.001		
Having sneezing											
No	14,406	97.4%	1308	96.6%	91 (86, 96)	1192	97.2%	83 (78, 87)	116	90.6%	8 (7, 10)
Yes	377	2.6%	46	3.4%	122 (91, 159)	34	2.8%	90 (63, 124)	12	9.4%	32 (17, 55)
p value			0.038			0.605			< 0.001		
Having sore throat											
No	14,206	96.1%	1161	85.7%	82 (77, 86)	1078	87.9%	76 (72, 80)	83	64.8%	6 (5, 7)
Yes	577	3.9%	193	14.3%	334 (296, 375)	148	12.1%	256 (221, 294)	45	35.2%	78 (57, 103)
p value			< 0.001			< 0.001			< 0.001		
Having irritation in the throat											
No	14,104	95.4%	1206	89.1%	86 (81, 90)	1120	91.4%	79 (75, 84)	86	67.2%	6 (5, 8)
Yes	679	4.6%	148	10.9%	218 (187, 251)	106	8.6%	156 (130, 186)	42	32.8%	62 (45, 83)
p value			< 0.001			< 0.001			< 0.001		
Having fever											
No	2,392	16.2%	235	17.4%	98 (87, 111)	233	19.0%	97 (86, 110)	2	1.6%	1 (0, 3)
Yes	12,391	83.8%	1119	82.6%	90 (85, 95)	993	81.0%	80 (75, 85)	126	98.4%	10 (8, 12)
p value			0.218			0.005			< 0.001		
Having headache											
No	5,918	40.0%	446	32.9%	75 (69, 82)	418	34.1%	71 (64, 77)	28	21.9%	5 (3, 7)
Yes	8,865	60.0%	908	67.1%	102 (96, 109)	808	65.9%	91 (85, 97)	100	78.1%	11 (9, 14)
p value			< 0.001			< 0.001			< 0.001		
Having retero orbital pain											
No	13,964	94.5%	1238	91.4%	89 (84, 93)	1119	91.3%	80 (76, 85)	119	93.0%	9 (7, 10)
Yes	819	5.5%	116	8.6%	142 (118, 167)	107	8.7%	131 (108, 156)	9	7.0%	11 (5, 21)
p value			< 0.001			< 0.001			0.459		
Having muscle pain											
No	13,292	89.9%	1035	76.4%	78 (73, 83)	970	79.1%	73 (69, 78)	65	50.8%	5 (4, 6)
Yes	1,491	10.1%	319	23.6%	214 (193, 236)	256	20.9%	172 (153, 192)	63	49.2%	42 (33, 54)
p value			< 0.001			< 0.001			< 0.001		
Having painful joints											
No	13,223	89.4%	994	73.4%	75 (71, 80)	971	79.2%	73 (69, 78)	23	18.0%	2 (1, 3)
Yes	1,560	10.6%	360	26.6%	231 (210, 252)	255	20.8%	163 (145, 183)	105	82.0%	67 (55, 81)
p value			< 0.001			< 0.001			< 0.001		
Having urge to vomit											
No	14,204	96.1%	1214	89.7%	85 (81, 90)	1129	92.1%	79 (75, 84)	85	66.4%	6 (5, 7)
Yes	579	3.9%	140	10.3%	242 (207, 279)	97	7.9%	168 (138, 200)	43	33.6%	74 (54, 99)
p value			< 0.001			< 0.001			< 0.001		
Having vomiting											
No	12,826	86.8%	975	72.0%	76 (71, 81)	975	79.5%	76 (71, 81)	0	0.0%	0 (0, 0)
Yes	1,957	13.2%	379	28.0%	194 (176, 212)	251	20.5%	128 (114, 144)	128	100.0%	65 (55, 77)
p value			< 0.001			< 0.001			< 0.001		
Having swelling in the body											
No	14,139	95.6%	1243	91.8%	88 (83, 93)	1129	92.1%	80 (75, 84)	114	89.1%	8 (7, 10)
Yes	644	4.4%	111	8.2%	172 (144, 204)	97	7.9%	151 (124, 181)	14	10.9%	22 (12, 36)
p value			< 0.001			< 0.001			< 0.001		
Having rashes											
No	14,379	97.3%	1230	90.8%	86 (81, 90)	1175	95.8%	82 (77, 86)	55	43.0%	4 (3, 5)
Yes	404	2.7%	124	9.2%	307 (262, 354)	51	4.2%	126 (95, 163)	73	57.0%	181 (144, 222)
p value			< 0.001			0.001			< 0.001		

The table shows the association and positivity rate of dengue and its subtypes with respiratory and dengue symptoms among dengue suspects in the study area.

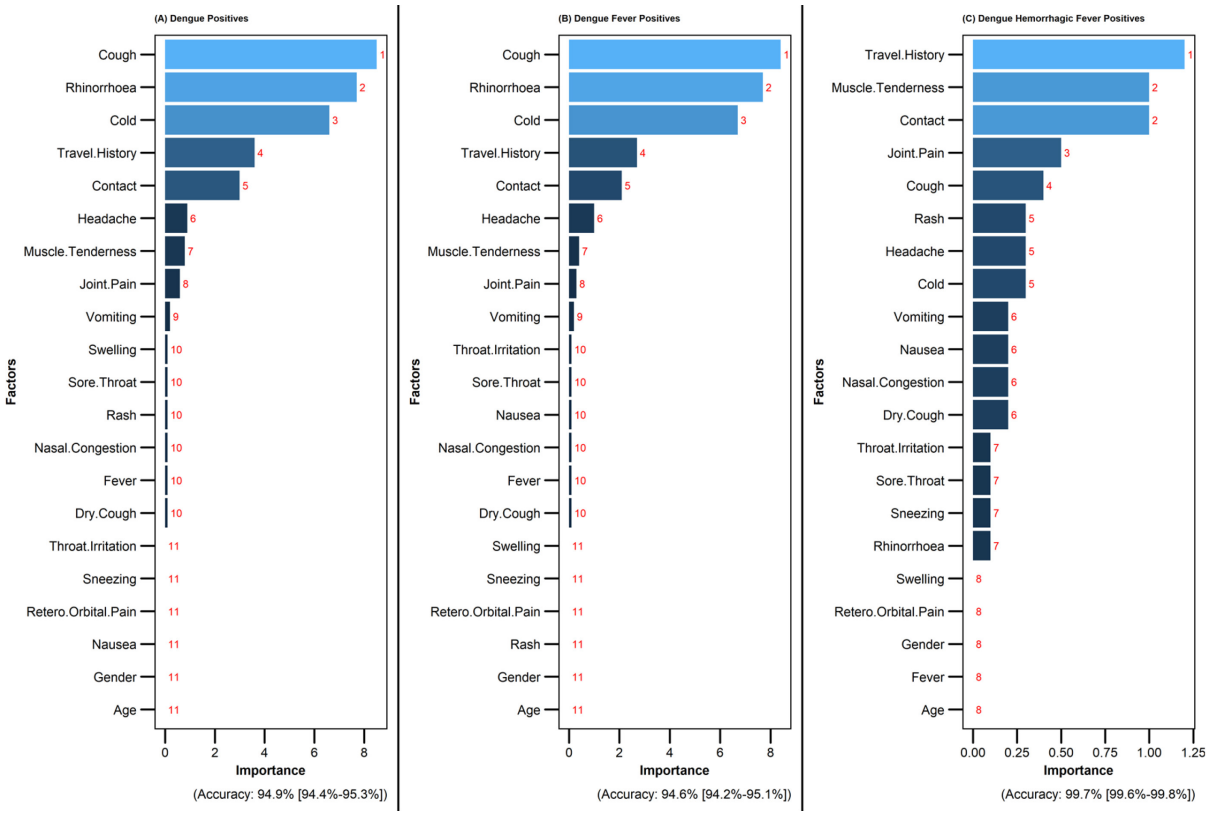
respiratory and dengue symptoms directly correlated with an increase in positive rates (Table 1). The findings of fever symptoms were comparable to dengue infection; however, this was not true for dengue hemorrhagic fever, since it was not related to age and gender. The positivity rate in those aged up to 15 years and those between 16 and 30 years were high [100 (95% CI: 91, 109) and 115 (95% CI: 105, 125), respectively].

Among the dengue suspected, 7927 (53.6%) were males and 8624 (58.4%) were under the age of 30 years at the time of diagnosis. There were 5177 (35.0%) and 4736 (32.0%) participants who reported having contact with patients who had similar symptoms in their households and communities respectively. There were 12,539 (84.8%) subjects who reported dengue symptoms, of which 3,377 (22.8%) had respiratory discomfort (Table 1).

Dengue suspects who reported various respiratory symptoms, including rhinorrhea 420 (95% CI: 395, 444), cold 333 (95% CI: 312, 355), cough 312 (95% CI: 293, 332), sore throat 334 (95% CI: 296, 375), and dry cough 363 (95% CI: 306, 424); had a high dengue positivity rate. Moreover, those who reported dengue symptoms, such as muscle pain 214 (95% CI: 193, 236), joint pain 231 (95% CI: 210, 252), body swelling 172 (95% CI: 144, 204), eye pain 142 (95% CI: 118, 167), and vomiting 194 (95% CI: 176, 212); also had high positive rates for dengue. The proportion of these respiratory and dengue symptoms was similar for dengue fever (Table 2).

Almost all the identified factors were significantly associated with dengue. Having cold, cough, dry cough, sore throat, rash, joint pain, nausea, and muscle tenderness had higher odds of being dengue positive. Having rash, joint pain, nasal congestion, and dry cough had much higher odds of being dengue hemorrhagic fever (Supplementary Table 1). Random forest (RF) analysis was performed to grade the factors to assess their importance in identifying dengue-positive cases among the suspected subjects. This grading had an accuracy of more than 90% for classifying dengue among the suspects and showed the sequence of the important factors that help in identifying dengue at the initial stages: the presence of cough, rhinorrhea, cold, travel history, dengue contacts, headache, muscle tenderness, and joint pain were the significant determinants for dengue fever. Having travel history, dengue contacts, presence of muscle tenderness, joint pain, and rash were the key determinants for dengue hemorrhagic fever (Figure 2).

Figure 2. The importance of factors in diagnosing dengue among dengue suspects.



Random-forest analysis plot reveals the significance of demographic factors, and respiratory and dengue symptoms in diagnosing dengue among suspects.

Discussion

Dengue in South Andaman has infiltrated into urban areas of Port Blair, mainly due to the widespread distribution of *Aedes aegypti*, the vector mosquito. Almost 26 dengue cases were reported in the year 2011 [18], which increased in number and severity and reached 1353 cases during the years 2018–2022. Dengue exhibits a wide range of symptoms, from mild fever to severe dehydration and even death as in classical dengue, depending on the severity of infection and the patient's exposure to the virus [4].

The findings from the present study were in line with earlier reports. The highest risk of dengue infection was observed between the ages of 16 and 30 years. The age group of 15 to 34 years was the most affected in Singapore, Vietnam, and Hanoi city [29–32]. Compared to the lower age groups, those who were ≥ 45 years had lower odds of dengue. This observed phenomenon might be explained by the propensity of older people to prioritize health, and hence follow more precautionary measures than young adults. Using bed nets / repellents every day during the daytime, for instance, would be an ideal example [32].

The age group 16 to 30 years had a two-fold higher odds ratio of dengue positives than those over 45 years. It is conceivable that a higher proportion of elderly people have already experienced at least one episode of dengue infection and could have developed immunity. This would have made them less likely to succumb to infection with the same dengue virus serotype [31]. Additionally, young people are more likely to reside in unhygienic environments, have lack of knowledge on dengue, and thus follow fewer preventive measures. They also spend more time participating in outdoor activities, increasing their likelihood of coming into contact with infective vectors outdoors [31,32].

The present study also found that males had a significantly higher odds of having dengue than females [29,31]. This observation was consistent with studies from South Asia [29]. In India, working adults, primarily men, are more likely to seek medical attention. Another significant factor to be considered is that men constitute a large proportion of the workforce, and they are more exposed to infective mosquito bites than women folks due to their occupational environment [33].

The dengue virus was prevalent in both rural and urban parts of the study area, as the mosquito vectors were abundant. The virus primarily disseminates in urban areas, where vectors have easy access to clean water source, thus facilitating breeding and proliferation [34,35]. Dengue outbreaks can be more severe in urban areas characterized by more clustering of human habitations [36,37]. The increase in urban population in numerous Southeast Asian nations can be attributed to the migration of people from rural settings for occupational reasons [36,38]. The mosquito species *Aedes aegypti* has evolved to thrive in densely populated areas by utilizing stagnant water sources in the premises of human habitation. Female *Aedes aegypti* mosquitoes prefer to blood feed on human hosts and are the primary vectors of dengue virus [39]; and thus, the presence of *Aedes aegypti* can lead to an increase in virus transmission. In view of the lack of specific treatment regimens, control of vector population is thus the key factor to reduce dengue outbreak risk in these urban areas.

The incidence of positive cases in urban areas within South Andaman differed significantly from rural areas. The dengue-infected persons will have a higher likelihood of transmitting the virus to the healthy and susceptible population through infective mosquito bites [40]. Cluster studies on dengue virus revealed localized transmission of DENV, a phenomenon observed among migrant populations [41].

Similar to the present study, a report from the Caribbean region concluded that fever is the primary symptom of dengue [42]. Most studies reported headache, muscle or joint pain, nausea, and rash as early symptoms; as observed in the present investigation [43,44]. Dengue-positive patients frequently reported respiratory symptoms such as cough, rhinorrhea, nasal stuffiness, and sore throat [45]. However, the presence of rhinorrhea in dengue positive patients was observed in this study. This finding aligns with earlier studies [11,46,47] suggesting that acute upper respiratory tract infection should be considered in the differential diagnosis of dengue infection.

Conclusions

There is no drug or vaccine available to treat DF/DHF. Mortality can be significantly reduced with early detection, proper case management, and symptomatic treatment [48,49]. Presumptive diagnosis with warning signs, fluid treatment guided with vital signs, and hematocrit levels should be monitored for dengue positive patients [48]. The present study shows that respiratory symptoms also need to be considered along with typical dengue-like symptoms to differentiate dengue. The results of the present study will help the health professionals distinguish dengue fever from other acute febrile illnesses by specific clinical characteristics [50]. This will facilitate in implementing early fluid therapy, thus reducing mortality rates [24] and disease burden due to dengue.

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Conflict of interest

No conflict of interest is declared.

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Annex – Supplementary Items

Supplementary Table 1. The odds ratios of factors for dengue infection, dengue fever, and dengue hemorrhagic fever.

Factors	Total dengue positive	Dengue fever (n)	Dengue hemorrhagic fever (n)
Age: 31–45 years	1.54[a] [1.26, 1.89]	1.59[a] [1.28, 1.97]	1.15 [0.62, 2.11]
Age: 16–30 years	2.25[a] [1.86, 2.71]	2.27[a] [1.86, 2.77]	1.82[c] [1.06, 3.12]
Age: ≤ 15 years	1.92[a] [1.58, 2.32]	1.99[a] [1.63, 2.45]	1.23 [0.70, 2.19]
Male gender	1.26[a] [1.13, 1.41]	1.28[a] [1.14, 1.44]	1.04 [0.74, 1.48]
Urban area	1.74[a] [1.54, 1.96]	1.70[a] [1.50, 1.93]	1.93[a] [1.30, 2.86]
Dengue contact	2.31[a] [2.07, 2.59]	2.34[a] [2.08, 2.63]	1.79[b] [1.26, 2.53]
Travel history	2.42[a] [2.16, 2.71]	2.44[a] [2.17, 2.75]	1.88[a] [1.327, 2.66]
Cold	8.35[a] [7.39, 9.43]	7.32[a] [6.45, 8.30]	12.35[a] [8.59, 17.75]
Cough	8.29[a] [7.36, 9.34]	7.03[a] [6.21, 7.95]	19.78[a] [13.04, 30.00]
Dry cough	6.02[a] [4.66, 7.78]	3.10[a] [2.30, 4.18]	28.89[a] [19.44, 42.93]
Nasal congestion	2.78[a] [2.17, 3.56]	0.89 [0.61, 1.30]	31.16[a] [21.61, 44.92]
Rhinorrhoea	13.26[a] [11.69, 15.03]	12.39[a] [10.89, 14.10]	8.81[a] [6.21, 12.51]
Sneezing	1.39[c] [1.02, 1.90]	1.10 [0.77, 1.57]	4.05[a] [2.22, 7.40]
Sore throat	5.65[a] [4.70, 6.78]	4.20[a] [3.45, 5.12]	14.39[a] [9.91, 20.90]
Throat irritation	2.98[a] [2.46, 3.61]	2.15[a] [1.73, 2.66]	10.75[a] [7.37, 15.67]
Fever	0.91 [0.79, 1.06]	0.81[b] [0.70, 0.94]	12.28[a] [3.04, 49.66]
Headache	1.40[a] [1.24, 1.58]	1.32[a] [1.17, 1.49]	2.40[a] [1.58, 3.65]
Retero-orbital pain	1.70[a] [1.38, 2.08]	1.73[a] [1.40, 2.13]	1.29 [0.65, 2.56]
Muscle tenderness	3.22[a] [2.81, 3.70]	2.63[a] [2.27, 3.06]	8.98[a] [6.32, 12.75]
Joint pain	3.69[a] [3.23, 4.22]	2.47[a] [2.12, 2.86]	41.42[a] [26.29, 65.24]
Nausea	3.41[a] [2.80, 4.16]	2.33[a] [1.86, 2.92]	13.33[a] [9.14, 19.42]
Vomiting	2.92[a] [2.56, 3.32]	1.79[a] [1.54, 2.07]	
Swelling	2.16[a] [1.75, 2.67]	2.04[a] [1.63, 2.56]	2.73[a] [1.56, 4.79]
Rashes	4.73[a] [3.80, 5.90]	1.62[b] [1.20, 2.19]	57.44[a] [39.81, 82.87]

The table presents odds ratios (ORs) with 95% confidence intervals (CIs) for factors associated with dengue infection, dengue fever, and dengue hemorrhagic fever. Values are shown as OR [95% CI]. Superscripts indicate levels of statistical significance: [a]$p < 0.001$, [b]$p < 0.01$, [c]$p < 0.05$.